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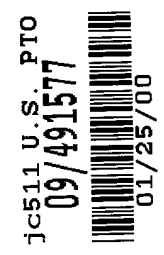
PATENT

ATTORNEY DOCKET NO.: 044574-5061-US

Express Mail No.: EI149177978US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Assistant Commissioner for Patents
Box Patent Application
Washington, D.C. 20231



09/491577

NEW APPLICATION TRANSMITTAL

Transmitted herewith for filing is the patent application of:

Inventor(s): **John R. CARLSON,**
Junhyong KIM,
Peter J. CLYNE,
Coral G. WARR,

For: NOVEL FAMILY OF ODORANT RECEPTORS IN DROSOPHILA

1. This new application is for a:
☒ Utility ☐ Design ☐ Plant
2. Papers enclosed which are required for a filing date:
77 Pages of specification including
1 Title Page
6 Pages of claims and
1 Page(s) of Abstract
6 Sheets of ☐ FORMAL ☒ INFORMAL drawings containing
29 Figures

☐ The enclosed drawing(s) are photograph(s), and there is also attached a
PETITION TO ACCEPT PHOTOGRAPH(S) AS DRAWING(S)
3. Combined Declaration and Power of Attorney
☐ Enclosed - and is executed by all inventors
☒ Not Enclosed
This application is being filed under the provisions of 37 C.F.R. §1.53(d).
Applicant(s) await notification from the Patent and Trademark Office of the time
set for filing the Declaration and paying the filing fees.

044574-5061-US

4. Language

- ☒ English
☐ Non-English

This application is being filed in accordance with 37 C.F.R. §1.52(d) and §608.01 of the MPEP. Applicant(s) await notification from the Patent and Trademark Office of the time set for filing the verified English translation and the processing fee.

5. Assignment

- ☐ is attached and Assignment of the invention is to _____
☐ also enclosed is the Form PTO 1595, Recordation Form Cover Sheet.

☒ will be filed at a later date

6. Certified Copy

Application(s) from which priority is claimed are:

Country	Application No.	Filed
United States	60/117,132	January 25, 1999

Certified copy(ies) is/are ☐ attached ☐ will follow

7. Fee Calculation

CLAIMS AS FILED				
	Number Filed	Number Extra	at Rate of	Basic Fee Utility\$760.00 Design\$310.00
Total Claims (37 CFR 1.16(c))	- 20 =		\$ 18.00 each=	+
Independent Claims (37 CFR 1.16(b))	- 3 =		\$ 78.00 each=	+
Multiple dependent claim(s), if any (37 CFR 1.16(d))			\$260.00	+
SUB-TOTAL =				
Reduction by 1/2 for filing by a small entity				- \$
TOTAL FILING FEE =				\$

8. Small Entity Statement(s)

- ☐ Verified Statement(s) that this is a filing by a small entity under 37 C.F.R. §1.9 and §1.27 is(are) attached.

9. Fee Payment

- ☒ Not Enclosed.

NO FEE IS BEING PAID BY CHECK OR DEPOSIT ACCOUNT AT THIS TIME.

This application is being filed under the provisions of 37 C.F.R. §1.53(d).
Applicant(s) await notification from the Patent and Trademark Office of the time set for filing the Declaration and paying the filing fees.

- ☐ Enclosed.

A check in the amount of \$_____ representing the filing fee of \$_____ and an assignment recording fee of \$_____ is enclosed.

Except for issue fees payable under 37 C.F.R. §1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 CFR §1.16 and §1.17 which may be required, or credit any overpayment to Deposit Account 50-0310.

10. Additional papers enclosed.

- ☐ Preliminary Amendment
☐ Information Disclosure Statement and Form PTO-1449
☐ Citations
☐ Declaration of Biological Deposit
☒ Submission of "Sequence Listing", computer readable copy and/or amendment pertaining thereto for biotechnology invention containing nucleotide and/or amino acid sequence.

Please accord an application number and filing date.

Respectfully submitted,

MORGAN, LEWIS & BOCKIUS LLP

Erich E. Veitenheimer
Erich E. Veitenheimer
Reg. No. 40,420

Dated: January 25, 2000
MORGAN, LEWIS & BOCKIUS LLP
1800 M Street, N.W.
Washington, D.C. 20036
(202) 467-7000

NOVEL ODORANT RECEPTORS IN DROSOPHILA

INVENTORS: John R. Carlson, Junhyong Kim, Peter J. Clyne, Coral G. Warr

5 RELATED APPLICATIONS

This application claims priority to U.S. provisional patent application Serial No. 60/117,132 filed January 25, 1999 which is herein incorporated by reference in its entirety.

10 U.S. GOVERNMENT SUPPORT

This work was supported by a grant from the National Institutes of Health (DC-02174).

FIELD OF THE INVENTION

15 This invention pertains to novel olfactory receptors and to methods of using such receptors. More particularly, this invention pertains to the nucleic acids and amino acids of novel olfactory receptors in *Drosophila* and to methods of using such nucleic acids and amino acids.

20 BACKGROUND OF THE INVENTION

Animals can detect a vast array of odors with remarkable sensitivity and discrimination. Olfactory information is first received by olfactory receptor neurons (olfactory receptors), which transmit signals into the central nervous system (CNS) where they are processed, ultimately leading to behavioral responses. An enormous amount of
25 investigation into olfactory function, organization, and development has been carried out in insect model systems for many years (Kaissling *et al.*, (1987) Ann. NY Acad. Sci. 510, 104-112; Hildebrand (1995) Proc. Natl. Acad. Sci. USA 92, 67-74). However, a number of central questions have been refractory to incisive analysis because the receptor

molecules to which odor molecules bind have not been identified, in any insect.

To investigate the molecular mechanisms of olfactory function and development, applicants studied the olfactory system of *Drosophila melanogaster*, which is highly sensitive and capable of odor discrimination (Siddiqi, (1991) Olfaction in *Drosophila*, in: Wysocki & Kare (ed.), Chemical Senses, Marcel Dekker; Carlson (1996) Trends Genet. 12, 175-180). There are two olfactory organs on the adult fly, the third segment of the antenna and the maxillary palp (Figure 1A). In both organs, olfactory receptors are housed in sensory hairs called sensilla. The organization of the approximately 1200 olfactory receptors of the antenna is complex but ordered. On the antenna there are different morphological categories of sensilla: s. trichodea, s. coeloconica, large s. basiconica, and small s. basiconica (Figure 1B). The different morphological categories of sensilla are distributed in overlapping patterns across the surface of the antenna (Figures 1C-F) (Venkatesh & Singh, (1984) Int. J. Insect Morphol. Embryol. 13, 51-63; Stocker, (1994) Roux's Arch. Dev. Biol. 205, 62-72).

Electrophysiological studies show that each morphological category of sensilla can be divided into different functional types (denoted by different colors in Figures 1C-F), defined by the characteristic response profiles of their olfactory receptors (Rodrigues *et al.*, (1991) Mol. Gen. Genet. 226, 265-276; Clyne *et al.*, (1997) Invert. Neurosci. 3, 127-135; de Bruyne *et al.*, unpublished results). For s. trichodea, the different functional types are segregated into zones on the surface of the antenna (Figure 1C); segregation is also observed for the different functional types of s. coeloconica (Figure 1D). This zonal organization is less conspicuous for the large and small s. basiconica, of which different functional types are intermingled (Figures 1E-F). Electrophysiological data suggest that there are on the order of thirty different classes of olfactory receptors in the antenna, a rough estimate based upon the odor response profiles of individual olfactory receptors (and in a few cases, the assumption that the neurons of particular functional types of sensilla have unique response profiles).

In contrast to the antenna, the organization of the approximately 120 olfactory

receptors of the maxillary palp is less complex. There are approximately 60 s. basiconica on the maxillary palp, each housing two olfactory receptors (Singh & Nayak, (1985) Int. J. Insect Morphol. Embryol. 14, 291-306). The 120 olfactory receptors fall into six different classes based upon their odorant response profiles (Clyne *et al.*, (1999) Neuron 22, 339-347; de Bruyne *et al.*, (1999) J. Neurosci. 19, 4520-4532). Neurons of the six ORN classes are always found in characteristic pairs in three functional types of s. basiconica, with the total number of neurons in each class being equal. Each class is distributed broadly over all, or almost all, of the olfactory surface of the maxillary palp.

Thus electrophysiological and anatomical studies suggest that there are on the order of thirty-five classes of olfactory receptors in the adult fly (approximately thirty on the antenna and six on the palp), each class with a distinct odor sensitivity. Classes of olfactory receptors found in the antenna are arrayed in zones, while the classes of olfactory receptors found in the maxillary palp are distributed in a less ordered fashion. olfactory receptors in both the maxillary palp and the antenna extend their axons to the antennal lobe of the brain, where first-order processing of olfactory information occurs. The lobe contains approximately forty olfactory glomeruli, spheroidal modules where ORN axons converge and where their terminal branches form synapses with the dendrites of their target interneurons (Stocker, (1994) Cell Tissue Res. 275, 3-26; Hildebrand & Shepherd, (1997) Annu. Rev. Neurosci. 20, 595-631).

One possibility underlying the molecular basis for distinct odor sensitivities for different classes of olfactory receptors is that each class of ORN expresses a unique odorant receptor, as has been proposed for vertebrate olfactory systems (Ngai *et al.*, (1993) Cell 72, 667-680; Ressler *et al.*, (1993) Cell 73, 597-609; Vassar *et al.*, (1993) Cell 74, 309-318; Buck, (1996) Annu. Rev. Neurosci. 19, 517-544; Hildebrand & Shepherd, (1997) Annu. Rev. Neurosci. 20, 595-631). Alternatively, each class of ORN might express a unique combination of a large set of receptors, as found in chemosensory cells of the nematode, *C. elegans* (Troemel *et al.*, (1995) Cell 83, 207-218). Both models call for a family of receptor genes, and several lines of evidence suggest that for insects such a

family would belong to the superfamily of seven-transmembrane G protein-coupled receptors (GPCRs). First, there is evidence that insects generate responses to odorants via GPCR-activated second-messenger systems. For example, a rapid and transient increase in inositol 1,4,5-trisphosphate (IP₃) has been observed in response to stimulation with

5 pheromone and other odors using antennal preparations from various insect species (Breer *et al.*, (1990) *Nature* 345, 65-68; Boekhoff *et al.*, (1993) *Insect Biochem. Mol. Biol.* 23, 757-762; Wegener *et al.*, (1993) *J. Insect Physiol.* 39, 153-163). This increase in IP₃ can be blocked by pertussis toxin, implicating a G protein signaling cascade (Boekhoff *et al.*, (1990) *Cell. Signal.* 2, 49-56). In *Drosophila*, *norpA* mutants, which lack the

10 phospholipase C that is an essential component of phototransduction, also exhibit reduced olfactory responses of the maxillary palp (Riesgo-Escovar *et al.*, (1995) *J. Comp. Physiol.* A180, 151-160). A second reason to suspect that odorant receptors in *Drosophila* are GPCRs is that GPCRs have been shown to be odorant receptors in both vertebrates and *C. elegans*; moreover, abundant evidence indicates that olfactory information in these other

15 organisms is transduced by GPCR-activated second messenger systems (Buck, (1996) *Annu. Rev. Neurosci.* 19, 517-544; Bargmann & Kaplan, (1998) *Annu. Rev. Neurosci.* 21, 279-308). It would thus seem unlikely that a family of receptors that have a completely novel structure and that use a completely different transduction mechanism would have arisen in insects.

20 There have been extensive efforts to identify odorant and pheromone receptors in a variety of insects using a wide range of strategies. These efforts have been driven in part by interest in analyzing receptor genes in the context of highly tractable experimental systems in which there is a wealth of knowledge about olfactory function and organization. For example, *Drosophila* offers the advantages of a model genetic

25 organism together with the ability to measure olfactory function conveniently *in vivo*, through either physiological or behavioral means. Interest in insect odorant receptors has also arisen because of the critical role of olfaction in the attraction of many insect pests to their plant hosts, of insect vectors of disease to their human hosts, and of insects to their

mates. Nevertheless, efforts to identify odorant receptors in insects, based upon searches for genes bearing sequence similarities to odorant receptor genes from other organisms, or on other strategies, have been unsuccessful.

Applicants have discovered a novel multigene family encoding candidate odorant receptors that were identified from the *Drosophila* genomic sequence database. The forty-nine genes described here were discovered using novel computer programs that identify diagnostic features of the protein structure of the seven-transmembrane GPCR superfamily. Members of this new family are highly divergent from previously defined genes. Nearly all of the genes are found to be expressed in one or both of the olfactory organs, and for a number of genes expression is restricted to a subset of olfactory receptors. Applicant's further demonstrate that expression of different genes is initiated at different times during the development of the adult antenna, and that expression of a subset of these candidate receptor genes depends on the POU domain transcription factor, Acj6 (abnormal chemosensory jump 6).

SUMMARY OF THE INVENTION

This invention provides isolated nucleic acid molecules including the following:

- a) isolated nucleic acid molecules that encode the amino acid sequences of *Drosophila* Odorant Receptor proteins;
- b) isolated nucleic acid molecules that encode protein fragments of at least 6 amino acids of a *Drosophila* Odorant Receptor proteins; and
- c) isolated nucleic acid molecules which hybridize to nucleic acid molecules which include nucleotide sequences encoding *Drosophila* Odorant Receptor proteins under conditions of sufficient stringency to produce a clear signal.

This invention also provides such isolated nucleic acid molecules wherein the nucleic acids include at least one exon-intron boundary located in one of the following positions:

- a) the nucleotides encoding the amino acids which include the third extracellular

domain of a *Drosophila* Odorant Receptor protein;

b) the nucleotides encoding the amino acids which include the fourth extracellular domain of a *Drosophila* Odorant Receptor protein; and

c) the nucleotides encoding the amino acids which include the fourth intracellular domain of a *Drosophila* Odorant Receptor protein.

This invention further provides such isolated nucleic acid molecules which have the nucleic acid sequence of one of the following sequences: SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95 and 97.

This invention also provides such isolated nucleic acid molecules operably linked to one or more expression control elements.

This invention further provides vectors which include any of the aforementioned nucleic acid molecules and host cells which include such vectors..

This invention also provides host cells transformed so as to contain any of the aforementioned nucleic acid molecules, wherein such host cells can be either prokaryotic host cells or eukaryotic host cells.

This invention also provides methods for producing proteins or protein fragments wherein the methods include transforming host cells with any of the aforementioned nucleic acids under conditions in which the protein or protein fragment encoded by said nucleic acid molecule is expressed. This invention also provides such methods wherein the host cells are either prokaryotic host cells or eukaryotic host cells. This invention further provides isolated proteins or protein fragments produced by such methods.

This invention provides isolated proteins or protein fragments which include:

a) isolated proteins encoded by one of the following amino acid sequences: SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96 and 98;

b) isolated protein fragments which include at least 6 amino acids of any of the

following sequences: SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96 and 98;

5 c) isolated proteins which include conservative amino acid substitutions of any of the following sequences: SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96 and 98; and

10 d) naturally occurring amino acid sequence variants of any of the following sequences: SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96 and 98.

The present invention further provides such isolated proteins or protein fragments which include at least one of the following conserved amino acids:

15 a) Leucine in the third extracellular domain of a *Drosophila* Odorant Receptor protein;

b) Histidine in the third extracellular domain of a *Drosophila* Odorant Receptor protein;

c) Cysteine in the sixth transmembrane domain of a *Drosophila* Odorant Receptor protein;

20 d) Tryptophan in the fourth extracellular domain of a *Drosophila* Odorant Receptor protein;

e) Glutamine in the seventh transmembrane domain of a *Drosophila* Odorant Receptor protein;

25 f) Proline in the seventh transmembrane domain of a *Drosophila* Odorant Receptor protein;

g) Alanine in the fourth intracellular domain of a *Drosophila* Odorant Receptor protein; and

h) Tyrosine in the fourth intracellular domain of a *Drosophila* Odorant Receptor

protein.

The present invention also provides isolated antibodies that bind to any of the aforementioned polypeptides.

5 The present invention also provides such antibodies which are either monoclonal antibodies or polyclonal antibodies.

This invention also provides methods of identifying agents which modulate the expression of any of the aforementioned proteins or protein fragments by:

a) exposing cells which express the proteins or protein fragments to the agents;
and

10 b) determining whether the agent modulates expression of said proteins or protein fragments, thereby identifying agents which modulate the expression of the proteins or protein fragments.

The present invention also provides methods of identifying agents which modulate the activity of any of the aforementioned proteins or protein fragments by:

15 a) exposing cells which express the proteins or protein fragments to the agents;
and

b) determining whether the agents modulate the activity of said proteins or protein fragments, thereby identifying agents which modulate the activity of the proteins or protein fragments.

20 The present invention also provides such methods where the agent modulates at least one activity of the proteins or protein fragments.

This invention provides methods of identifying agents which modulate the transcription of any of the aforementioned nucleic acid molecules by:

a) exposing cells which transcribe the nucleic acids to the agents; and
25 b) determining whether the agents modulate transcription of said nucleic acids, thereby identifying agents which modulate the transcription of the nucleic acid.

This invention further provides methods of identifying binding partners for the aforementioned proteins or protein fragments by:

- a) exposing said proteins or protein fragments to potential binding partners; and
- b) determining if the potential binding partners bind to said proteins or protein fragments, thereby identifying binding partners for the proteins or protein fragments.

The present invention also provides methods of modulating the expression of nucleic acids encoding the aforementioned proteins or protein fragments by administering an effective amount of agents which modulate the expression of the nucleic acids encoding the proteins or protein fragments.

This invention also provides methods of modulating at least one activity of the aforementioned proteins or protein fragments by administering an effective amount of the agents which modulate at least one activity of the proteins or protein fragments.

This invention provides methods of identifying novel olfactory receptor genes by:

- a) selecting candidate olfactory receptor genes by screening nucleic acid databases using an algorithm trained to identify seven transmembrane receptors genes;

- b) screening said selected candidate olfactory receptor genes by identifying nucleic acid sequences with conserved amino acid residues and intron-exon boundaries common to olfactory receptors, and having open reading frames of sufficient size so as to encode a seven transmembrane receptor; and

- c) identifying the novel olfactory receptor genes and measuring the expression of olfactory receptor genes wherein the detection of expression confirms said candidate olfactory genes as olfactory genes.

This invention also provides methods of identifying novel olfactory receptor genes by:

- a) selecting candidate olfactory receptor genes by screening nucleic acid databases for nucleic acid sequences with sufficient homology to at least one known olfactory receptor gene;

- b) screening said selected candidate olfactory receptor genes by identifying nucleic acids with conserved amino acid residues and intron-exon boundaries common to olfactory receptors, and having open reading frames of sufficient size so as to encode a

seven transmembrane receptor; and

c) identifying the novel olfactory receptor genes and measuring the expression of olfactory receptor genes wherein the detection of expression confirms said candidate olfactory genes as olfactory genes.

5 The present invention also provides transgenic insects modified to contain any of the aforementioned nucleic acid molecules.

This invention also provides such transgenic insects, wherein the nucleic acid molecules contain mutations that alter expression of the encoded proteins.

10 **BRIEF DESCRIPTION OF THE DRAWINGS**

Figure 1 An overview of the olfactory system of the adult *Drosophila*. (A) The two olfactory organs of the adult fly, the third antennal segment (arrow) and the maxillary palp (arrowhead), scale bar = 100 μ m. (B) Higher magnification of part of a third antennal segment showing the morphological categories of olfactory sensilla: s. basiconica [B], s. trichodea [T] and s. coeloconica [C], scale bar = 5 μ m. (C-F) Diagram of the olfactory sensilla on the anterior face of the third antennal segment. The different morphological categories of sensilla are indicated by different shapes, and the colors indicate different functional types of sensilla within each morphological category. Dorsal is at the top and medial is to the left. (C) Distribution of different functional types of s. trichodea. (D) Distribution of different functional types of s. coeloconica. (E) The large s. basiconica are densely clustered in a small dorso-medial region, where the different functional types are intermingled. For simplicity, only two types are shown. (F) The small s. basiconica are widely dispersed, and the different functional types are intermingled.

25

Figure 2 Genomic organization and hydropathy plots of DOR genes. (A) Genomic organization of DOR genes (not to scale). The genes shown are those identified from 16% of the total genomic sequence; most of the available sequence is from Chromosome

2. The approximate chromosomal location of each gene is indicated. Genes separated by less than one kilobase are jointly underlined. Within each cluster, all genes are oriented in the same direction. The transcriptional orientation of the DOR genes with respect to the chromosome is unknown for 2F.1, 25A.1, 47E.2, 59D.1, and the cluster at 33B. (B) The 2F.1 gene is flanked by two closely linked genes, *fs(1)k10* and *crn*. The arrowheads indicate the 3' end of each gene; for 2F.1 the end of the arrow indicates the position of the polyA+ addition signal sequence. (C) Hydropathy plots of the genes whose expression patterns are shown in Figures 4-6. Hydrophobic peaks predicted by Kyte-Doolittle analysis appear above the center line. The approximate positions of the seven putative transmembrane domains are indicated above the first hydropathy plot.

Figure 3 Amino acid sequence alignment of DOR genes. All DNA sequences were obtained from the BDGP database, and the determination of predicted amino acid sequences is described in the Examples. Residues conserved in >50% of the predicted proteins are shaded. The approximate locations of predicted transmembrane domains 1-7 are indicated. Exon-intron boundaries are shown with vertical lines.

Figure 4 DOR genes are expressed in subsets of olfactory receptor neurons in the maxillary palp. *In situ* hybridizations to tissue sections of maxillary palps. Panel A shows a frontal section; all other sections are sagittal. (A) A 46F.1 probe reveals expression in a subset of olfactory receptors which are broadly distributed. The background staining at the periphery of the organ represents non-specific labeling of the cuticle, observed equally for sense and antisense probes. (B) A 33B.3 probe also hybridizes to a subset of cells. Unlabeled olfactory receptors are visible under the cuticular surface (top center). (C) At higher magnification it can be seen that the cells expressing 46F.1 are neurons. Note the axons projecting from the cells into the nerve (n) which runs through the middle of the maxillary palp. The arrowhead indicates an ORN which is not expressing 46F.1, adjacent to an ORN which is strongly stained. The light

staining of the nerve is background staining, observed equally for sense and antisense probes. (D) 33B.3 is not expressed in the *acj6* null mutant, *acj6*⁶.

Figure 5 DOR genes are expressed in subsets of antennal cells. Shown are *in situ* hybridizations to tissue sections of third antennal segments. In panels A, B, D, and F the plane of section passes through the fluid-filled interior of the antenna. (A,B) A 47E.1 probe hybridizes to a subset of cells which are broadly distributed. (C,D) A 25A.1 probe hybridizes to a smaller subset of cells. The angle of section in panel C differs somewhat from the other panels. (E) A 22A.2 probe hybridizes to a subset of cells in the dorso-medial region where the large s. basiconica are located. (F) 22A.2 is expressed in the *acj6*⁶ mutant, in contrast to 33B.3 (Figure 4D). (G) Summary of distributions of labeled cells for 47E.1 (open circles), 25A.1 (black dots), and 22A.2 (gray dots) on the anterior face of the antenna, based on analysis of expression in 30-50 antennae for each gene.

Figure 6 Expression of DOR genes during antennal development. *In situ* hybridizations to tissue sections of third antennal segments at different times during pupal development. The times indicated refer to hours APF (after puparium formation). Arrows indicate labeled cells. (A) Expression of 22A.2 is not observed at 54 hours APF. Note that background staining is absent in sections taken at 54 hours (or at earlier times), presumably due to the immaturity of the cuticle. (B) Expression of 22A.2 is observed at 60 hours APF. (C) 47E.1 expression is not observed at 72 hours APF. Background staining is observed with both sense and antisense probes on the cuticular surface of the sacculus (s), a multi-chambered sensory pit and the dot at the bottom of the third antennal segment is non-specific staining of a section of tracheal tissue. (D) Expression of 47E.1 is detected at 93 hours APF. (E) The odor binding protein OS-E is not expressed at 72 hours APF. The small dots at the bottom of the antenna are non-specific staining of a section of tracheal tissue, observed with both sense and antisense probes. (F) Abundant

expression of OS-E is seen at 93 hours APF.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

I. Specific Embodiments

5 A. *Drosophila* Olfactory Receptor Proteins

10 The present invention provides a family of isolated proteins, allelic variants of the proteins, and conservative amino acid substitutions of the proteins. As used herein, protein or polypeptide refers to any one of the proteins that has the amino acid sequence depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96 and 98. The invention also includes naturally occurring allelic variants and proteins that have a slightly different amino acid sequence than that specifically recited above. Allelic variants, though possessing a slightly different amino acid sequence than those recited above, will still have the same or similar biological functions associated with any of the amino acid proteins.

15 As used herein, the family of proteins related to any one of the amino acid sequences depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96 and 98 refers to proteins that have been isolated from organisms in addition to *Drosophila*. The methods used to identify and isolate other members of the family of proteins related to these amino acid proteins are described below.

20 The proteins of the present invention are preferably in isolated form. As used herein, a protein is said to be isolated when physical, mechanical or chemical methods are employed to remove the protein from cellular constituents that are normally associated with the protein. A skilled artisan can readily employ standard purification methods to obtain an isolated protein.

25 The proteins of the present invention further include conservative amino acid substitution variants (*i.e.*, conservative) of the proteins herein described. As used herein,

a conservative variant refers to at least one alteration in the amino acid sequence that does not adversely affect the biological functions of the protein. A substitution, insertion or deletion is said to adversely affect the protein when the altered sequence prevents or disrupts a biological function associated with the protein. For example, the overall charge, structure or hydrophobic-hydrophilic properties of the protein can be altered without adversely affecting a biological activity. Accordingly, the amino acid sequence can often be altered, for example to render the peptide more hydrophobic or hydrophilic, without adversely affecting the biological activities of the protein.

Ordinarily, the allelic variants, the conservative substitution variants, and the members of the protein family, will have an amino acid sequence having at least 30% amino acid sequence identity with the sequences set forth in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96 and 98 more preferably at least 35%, even more preferably at least 40%, and most preferably at least 45%. Identity or homology with respect to such sequences is defined herein as the percentage of amino acid residues in the candidate sequence that are identical with the known peptides, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent homology, and not considering any conservative substitutions as part of the sequence identity. N-terminal, C-terminal or internal extensions, deletions, or insertions into the peptide sequence shall not be construed as affecting homology.

In addition to amino acid sequence identity, the proteins of the present invention have seven transmembrane domains as defined by hydropathy analysis (Kyte & Doolittle, (1982) J. Mol. Biol. 157, 105-132). Furthermore, the proteins of the present invention have conserved amino acid residues in defined domains of the protein. For example, the proteins of the present invention have at least one of the following conserved amino acids as depicted in Figure 3, including but not limited to, Leucine in the third extracellular domain; Histidine in the third extracellular domain; Cysteine in the sixth transmembrane

domain; Tryptophan in the fourth extracellular domain; Glutamine in the seventh transmembrane domain; Proline in the seventh transmembrane domain; Alanine in the fourth intracellular domain; or Tyrosine in the fourth intracellular domain. In addition, the conserved amino acids may be selected from any of the amino acid residues indicated as being conserved among DOR proteins as depicted in Figure 3 (shaded).

Thus, the proteins of the present invention include molecules having the amino acid sequence disclosed in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96 and 98; fragments thereof having a consecutive sequence of at least about 3, 4, 5, 6, 10, 15, 20, 25, 30, 35 or more amino acid residues of the proteins, for instance, antigenic fragments such as those found in the extracellular domains of the protein (see Figure 3); amino acid sequence variants wherein an amino acid residue has been inserted N- or C-terminal to, or within, the disclosed sequence; and amino acid sequence variants of the disclosed sequences, or their fragments as defined above, that have been substituted by another residue. Contemplated variants further include those containing predetermined mutations by, *e.g.*, homologous recombination, site-directed or PCR mutagenesis, and the corresponding proteins of other insect species, including but not limited to the order *Diptera*, *Lepidoptera*, *Homoptera* and *Coleoptera*, within these orders, preferably the genus *Drosophila*, *Anopheles*, *Aedes*, *Ceratitis*, *Muscidae*, *Culicidae*, *Anagasta* and *Popilla* and the alleles or other naturally occurring variants of the family of proteins; and derivatives wherein the protein has been covalently modified by substitution, chemical, enzymatic, or other appropriate means with a moiety other than a naturally occurring amino acid (for example a detectable moiety such as an enzyme or radioisotope).

As described below, members of the family of proteins can be used: 1) to identify agents which modulate at least one activity of the protein; 2) to identify binding partners for the protein, 3) as an antigen to raise polyclonal or monoclonal antibodies, and 4) in methods to modify insect behavior.

B. Nucleic Acid Molecules

The present invention further provides nucleic acid molecules which encode any of the proteins having SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96 and 98 and the related proteins herein described, preferably in isolated form. As used herein, "nucleic acid" is defined as RNA or DNA that encodes a protein or peptide as defined above, is complementary to a nucleic acid sequence encoding such peptides, hybridizes to such a nucleic acid and remains stably bound to it under appropriate stringency conditions, or encodes a polypeptide sharing at least 75% sequence identity, preferably at least 80%, and more preferably at least 85%, with the peptide sequences in conserved domains. Specifically contemplated are genomic DNA, cDNA, mRNA and antisense molecules, as well as nucleic acids based on alternative backbones or including alternative bases whether derived from natural sources or synthesized. Such hybridizing or complementary nucleic acids, however, are defined further as being novel and non-obvious over any prior art nucleic acid including that which encodes, hybridizes under appropriate stringency conditions, or is complementary to nucleic acid encoding a protein according to the present invention.

Homology or identity at the amino acid or nucleotide level is determined by **BLAST** (Basic Local Alignment Search Tool) analysis using the algorithm employed by the programs **blastp**, **blastn**, **blastx**, **tblastn** and **tblastx** (Karlin *et al.*, (1990) Proc. Natl. Acad. Sci. USA 87, 2264-2268 and Altschul, (1993) J. Mol. Evol. 36, 290-300, fully incorporated by reference) which are tailored for sequence similarity searching. The approach used by the **BLAST** program is to first consider similar segments between a query sequence and a database sequence, then to evaluate the statistical significance of all matches that are identified and finally to summarize only those matches which satisfy a preselected threshold of significance. For a discussion of basic issues in similarity searching of sequence databases (see Altschul *et al.*, (1994) Nature Genetics 6, 119-129

which is fully incorporated by reference). The search parameters for **histogram**, **descriptions**, **alignments**, **expect** (*i.e.*, the statistical significance threshold for reporting matches against database sequences), **cutoff**, **matrix** and **filter** are at the default settings. The default scoring matrix used by **blastp**, **blastx**, **tblastn**, and **tblastx** is the

5 **BLOSUM62** matrix (Henikoff *et al.*, (1992) Proc. Natl. Acad. Sci. USA 89, 10915-10919, fully incorporated by reference). For **blastn**, the scoring matrix is set by the ratios of **M** (*i.e.*, the reward score for a pair of matching residues) to **N** (*i.e.*, the penalty score for mismatching residues), wherein the default values for **M** and **N** are 5 and -4, respectively.

10 “Stringent conditions” are those that (1) employ low ionic strength and high temperature for washing, for example, 0.5 M sodium phosphate buffer at pH 7.2, 1 mM EDTA at pH 8.0 in 7% SDS at either 65°C or 55°C, or (2) employ during hybridization a denaturing agent such as formamide, for example, 50% formamide with 0.1% bovine serum albumin, 0.1% Ficoll, 0.1% polyvinylpyrrolidone, 0.05 M sodium phosphate buffer
15 at pH 6.5 with 0.75 M NaCl, 0.075 M sodium citrate at 42°C. Another example is use of 50% formamide, 5× SSC (0.75 M NaCl, 0.075 M sodium citrate), 50 mM sodium phosphate at pH 6.8, 0.1% sodium pyrophosphate, 5× Denhardt’s solution, sonicated salmon sperm DNA (50 µg/ml), 0.1% SDS and 10% dextran sulfate at 55°C, with washes at 55°C in 0.2× SSC and 0.1% SDS. A skilled artisan can readily determine and vary the
20 stringency conditions appropriately to obtain a clear and detectable hybridization signal. Preferred molecules are those that hybridize under the above conditions to the complements of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95 and 97, and which encode a functional protein.

25 As used herein, a nucleic acid molecule is said to be “isolated” when the nucleic acid molecule is substantially separated from contaminant nucleic acid encoding other polypeptides from the source of nucleic acid.

The present invention further provides fragments of any one of the encoding nucleic

acids molecules. As used herein, a fragment of an encoding nucleic acid molecule refers to a small portion of the entire protein coding sequence. The size of the fragment will be determined by the intended use. For example, if the fragment is chosen so as to encode an active portion of the protein, the fragment will need to be large enough to encode the functional region(s) of the protein. For instance, fragments of the invention encode antigenic fragments such as the extracellular loops or N-terminal domain of the protein depicted in SEQ ID NO: 2 and as set forth in Figure 3. If the fragment is to be used as a nucleic acid probe or PCR primer, then the fragment length is chosen so as to obtain a relatively small number of false positives during probing and priming.

Fragments of the encoding nucleic acid molecules of the present invention (*i.e.*, synthetic oligonucleotides) that are used as probes or specific primers for the polymerase chain reaction (PCR), or to synthesize gene sequences encoding proteins of the invention can easily be synthesized by chemical techniques, for example, the phosphotriester method of Matteucci *et al.*, (1981) J. Am. Chem. Soc. 103, 3185-3191) or using automated synthesis methods. In addition, larger DNA segments can readily be prepared by well known methods, such as synthesis of a group of oligonucleotides that define various modular segments of the gene, followed by ligation of oligonucleotides to build the complete modified gene.

The encoding nucleic acid molecules of the present invention may further be modified so as to contain a detectable label for diagnostic and probe purposes. A variety of such labels are known in the art and can readily be employed with the encoding molecules herein described. Suitable labels include, but are not limited to, fluorescent-labeled, biotin-labeled, radio-labeled nucleotides and the like. A skilled artisan can employ any of the art known labels to obtain a labeled encoding nucleic acid molecule.

Modifications to the primary structure itself by deletion, addition, or alteration of the amino acids incorporated into the protein sequence during translation can be made without destroying the activity of the protein. Such substitutions or other alterations result in proteins having an amino acid sequence encoded by a nucleic acid falling within the contemplated scope of the present invention.

C. Isolation of Other Related Nucleic Acid Molecules

As described above, the identification and characterization of the nucleic acid molecules having SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95 and 97 allows a skilled artisan to isolate nucleic acid molecules that encode other members of the protein family in addition to the sequences herein described. Further, the presently disclosed nucleic acid molecules allow a skilled artisan to isolate nucleic acid molecules that encode other members of the family of proteins in addition to the protein having SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96 and 98.

Essentially, a skilled artisan can readily use any one of the amino acid sequences selected from SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96 and 98, to generate antibody probes to screen expression libraries prepared from appropriate cells. Typically, polyclonal antiserum from mammals such as rabbits immunized with the purified protein (as described below) or monoclonal antibodies can be used to probe a cDNA or genomic expression library to obtain the appropriate coding sequence for other members of the protein family. The cloned cDNA sequence can be expressed as a fusion protein, expressed directly using its own control sequences, or expressed by constructions using control sequences appropriate to the particular host used for expression of the enzyme.

Alternatively, a portion of the coding sequence herein described can be synthesized and used as a probe to retrieve DNA encoding a member of the protein family from any organism. Oligomers containing approximately 18-20 nucleotides (encoding about a six to seven amino acid stretch) are prepared and used to screen genomic DNA or cDNA libraries to obtain hybridization under stringent conditions or conditions of sufficient stringency to

eliminate an undue level of false positives.

Additionally, pairs of oligonucleotide primers can be prepared for use in a polymerase chain reaction (PCR) to selectively clone an encoding nucleic acid molecule. A PCR denature/anneal/extend cycle for using such PCR primers is well known in the art and can readily be adapted for use in isolating other encoding nucleic acid molecules. For example, degenerate primers can be used to clone any DOR gene across species. Specifically, based on the sequence information derived from the family of DORs, degenerate primers can be designed based on conserved sequences among olfactory receptors, which can then be used to clone nucleic acid molecules encoding olfactory receptor proteins from other species of insects.

Applicants have also identified a method for isolating nucleic acid molecules that encode other members of the protein family in addition to the sequences herein described. Essentially, a two-step strategy is employed to identify odorant receptor genes from the genomic database. First, a computer algorithm was designed to search genomic sequences for open reading frames (ORFs) from candidate odorant receptor genes. Second, RT-PCR is used to determine if transcripts from any of these ORFs are expressed in olfactory organs.

The algorithm is used to identify GPCR genes using statistical characterization of amino acid physico-chemical profiles in combination with a non-parametric discriminant function. The algorithm is trained on a set of putative sequences from a database. In the first step, three sets of descriptors are used to summarize the physico-chemical profiles of the sequences. These are GES scale of hydropathy (Engelman *et al.*, (1986) *Annu. Rev. Biophys. Biophys. Chem.* 15, 321-353), polarity (Brown, (1991) *Molecular Biology Labfax*, Academic Press), and amino acid usage frequency. For the first two of these measurements, a computed sliding window profile is employed (White, (1994) *Membrane Protein Structure*, Oxford University Press) using a kernel of a certain number of amino acids as a constant function convoluted with a certain number of amino acids as a Gaussian function. These profiles are then summarized with three statistics; the periodicity, average derivative and the variance of the derivative.

Each sequence is then characterized by multiple variables using a non-parametric linear discriminant function that is optimized to separate the known family proteins from random proteins in the training set. The same linear discriminant function with the scores derived from the training set is used to screen any nucleic acid database for candidate genes.

5 The candidate sequences are given significance values by an odds ratio of the proteins and non-family proteins, computed using the observed empirical distribution of the training set. Those sequences with a sufficiently high odds ratio are considered for further analysis. The algorithm can also be used to identify any protein family by altering the training set of sequences.

10 The method of identification further includes steps for identifying novel olfactory receptor genes comprising selecting candidate olfactory receptor genes by screening a nucleic acid database using an algorithm trained to identify seven transmembrane receptors genes; screening said selected candidate olfactory receptor genes by identifying nucleic acid sequences with conserved amino acid residues and intron-exon boundaries common to
15 olfactory receptors, and open reading frames of sufficient size as to encode a seven transmembrane receptor. As an additional step, the expression of olfactory receptor genes is measured to confirm candidate olfactory gene as an olfactory gene. The exon-intron boundaries and conserved amino acid residues may be selected from any of the positions depicted in Figure 3. Alternatively, selecting candidate olfactory receptor genes by screening
20 a nucleic acid database for nucleic acid sequences with sufficient homology to at least one known olfactory receptor gene is also encompassed in the invention. In a preferred embodiment, the nucleic acid database is a genomic database, an EST database or even an olfactory receptor database as previously described (Skoufos *et al.*, (1999) Nucleic Acids Research 27, 343-345).

25 In one example of the invention, the training set could consist of a subset of seven transmembrane proteins such as dopaminergic receptors and could be used to search genomic sequences for new subtypes of dopaminergic receptors. In another example, the training set could consist of ion channels and could be used to identify new subtypes of ion channels in a

particular family. In yet another example, the training set could consist of known sequences coding for a receptors from a particular family and could be used to identify homologs across species. Specifically, olfactory receptors of one species could be used as a training set to identify olfactory receptors in another species.

5

D. rDNA molecules containing a DNA molecule

The present invention further provides recombinant DNA molecules (rDNAs) that contain a coding sequence. As used herein, a rDNA molecule is a DNA molecule that has been subjected to molecular manipulation *in situ*. Methods for generating rDNA molecules are well known in the art, for example, see Sambrook *et al.*, (1985) Molecular Cloning - A Laboratory Manual, Cold Spring Harbor Laboratory Press. In the preferred rDNA molecules, a coding DNA sequence is operably linked to expression control sequences or vector sequences.

10

The choice of vector and expression control sequences to which one of the protein family encoding sequences of the present invention is operably linked depends directly, as is well known in the art, on the functional properties desired, *e.g.*, protein expression, and the host cell to be transformed. A vector contemplated by the present invention is at least capable of directing the replication or insertion into the host chromosome, and preferably also expression, of the structural gene included in the rDNA molecule.

15

Expression control elements that are used for regulating the expression of an operably linked protein encoding sequence are known in the art and include, but are not limited to, inducible promoters, constitutive promoters, secretion signals, and other regulatory elements. Preferably, the inducible promoter is readily controlled, such as being responsive to a nutrient in the host cell's medium.

20

In one embodiment, the vector containing a coding nucleic acid molecule will include a prokaryotic replicon, *i.e.*, a DNA sequence having the ability to direct autonomous replication and maintenance of the recombinant DNA molecule extra-chromosomally in a prokaryotic host cell, such as a bacterial host cell, transformed therewith. Such replicons are

25

well known in the art. In addition, vectors that include a prokaryotic replicon may also include a gene whose expression confers a detectable marker such as a drug resistance. Typical bacterial drug resistance genes are those that confer resistance to ampicillin or tetracycline.

5 Vectors that include a prokaryotic replicon can further include a prokaryotic or bacteriophage promoter capable of directing the expression (transcription and translation) of the coding gene sequences in a bacterial host cell, such as *E. coli*. A promoter is an expression control element formed by a DNA sequence that permits binding of RNA polymerase and transcription to occur. Promoter sequences compatible with bacterial hosts
10 are typically provided in plasmid vectors containing convenient restriction sites for insertion of a DNA segment of the present invention. Typical of such vector plasmids are pUC8, pUC9, pBR322 and pBR329 available from BioRad Laboratories, pPL and pKK223 available from Pharmacia.

 Expression vectors compatible with eukaryotic cells, preferably those compatible with
15 vertebrate cells such as insect cells, can also be used to form a rDNA molecules that contains a coding sequence. Eukaryotic cell expression vectors are well known in the art and are available from several commercial sources. Typically, such vectors are provided containing convenient restriction sites for insertion of the desired DNA segment. Typical of such vectors are pSVL and pKSV-10 (Pharmacia), pBPV-1/pML2d (International Biotechnologies, Inc.),
20 pTDT1 (ATCC, #31255), the vector pCDM8 described herein, and the like eukaryotic expression vectors. Vectors may be modified to include insect cell specific promoters if needed.

 Eukaryotic cell expression vectors used to construct the rDNA molecules of the present invention may further include a selectable marker that is effective in an eukaryotic
25 cell, preferably a drug resistance selection marker. A preferred drug resistance marker is the gene whose expression results in neomycin resistance, *i.e.*, the neomycin phosphotransferase (*neo*) gene (Southern *et al.*, (1982) J. Mol. Appl. Genet. 1, 327-341). Alternatively, the selectable marker can be present on a separate plasmid, and the two vectors are introduced by

co-transfection of the host cell, and selected by culturing in the appropriate drug for the selectable marker.

E. Host Cells Containing an Exogenously Supplied Coding Nucleic Acid

5 The present invention further provides host cells transformed with a nucleic acid molecule that encodes a protein of the present invention. The host cell can be either prokaryotic or eukaryotic. Eukaryotic cells useful for expression of a protein of the invention are not limited, so long as the cell line is compatible with cell culture methods and compatible with the propagation of the expression vector and expression of the gene product. Preferred
10 eukaryotic host cells include, but are not limited to, yeast, insect and mammalian cells, preferably insect cells such as those from a *Drosophila* cell line. Preferred *Drosophila* host cells include *Drosophila* Schneider line 2, and the like insect tissue culture cell lines.

Any prokaryotic host can be used to express a rDNA molecule encoding a protein of the invention. The preferred prokaryotic host is *E. coli*.

15 Transformation of appropriate cell hosts with a rDNA molecule of the present invention is accomplished by well known methods that typically depend on the type of vector used and host system employed. With regard to transformation of prokaryotic host cells, electroporation and salt treatment methods are typically employed, see, for example, Cohen *et al.*, (1972) Proc. Natl. Acad. Sci. USA 69, 2110-2114; and Maniatis *et al.*, (1982) Molecular
20 Cloning - A Laboratory Manual, Cold Spring Harbor Laboratory Press. With regard to transformation of vertebrate cells with vectors containing rDNAs, electroporation, cationic lipid or salt treatment methods are typically employed, see, for example, Graham *et al.*, (1973) Virology 52, 456-467; and Wigler *et al.*, (1979) Proc. Natl. Acad. Sci. USA 76, 1373-1376.

25 Successfully transformed cells, *i.e.*, cells that contain a rDNA molecule of the present invention, can be identified by well known techniques including the selection for a selectable marker. For example, cells resulting from the introduction of an rDNA of the present invention can be cloned to produce single colonies. Cells from those colonies can be harvested, lysed and their DNA content examined for the presence of the rDNA using a

method such as that described by Southern, (1975) J. Mol. Biol. 98, 503-517; or Berent *et al.*, (1985) Biotech. Histochem. 3, 208; or the proteins produced from the cell assayed via an immunological method.

5 F. Production of Recombinant Proteins using a rDNA Molecule

The present invention further provides methods for producing a protein of the invention using nucleic acid molecules herein described. In general terms, the production of a recombinant form of a protein typically involves the following steps: First, a nucleic acid molecule is obtained that encodes a protein of the invention, such as any of the nucleic acid molecule depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95 and 97. The nucleic acid molecule is then preferably placed in operable linkage with suitable control sequences, as described above, to form an expression unit containing the protein open reading frame. The expression unit is used to transform a suitable host and the transformed host is cultured under conditions that allow the production of the recombinant protein. Optionally the recombinant protein is isolated from the medium or from the cells; recovery and purification of the protein may not be necessary in some instances where some impurities may be tolerated.

Each of the foregoing steps can be done in a variety of ways. For example, the desired coding sequences may be obtained from genomic fragments and used directly in appropriate hosts. The construction of expression vectors that are operable in a variety of hosts is accomplished using appropriate replicons and control sequences, as set forth above. The control sequences, expression vectors, and transformation methods are dependent on the type of host cell used to express the gene and were discussed in detail earlier. Suitable restriction sites can, if not normally available, be added to the ends of the coding sequence so as to provide an excisable gene to insert into these vectors. A skilled artisan can readily adapt any host-expression system known in the art for use with the nucleic acid molecules of the invention to produce recombinant protein.

G. Methods to Identify Binding Partners

Another embodiment of the present invention provides methods for use in isolating and identifying binding partners of any of the DOR proteins of the invention. In detail, a protein of the invention is mixed with a potential binding partner or an extract or fraction of a cell under conditions that allow the association of potential binding partners with the protein of the invention. After mixing, peptides, polypeptides, proteins or other molecules that have become associated with a protein of the invention are separated from the mixture. The binding partner that bound to the protein of the invention can then be removed and further analyzed. To identify and isolate a binding partner, the entire protein, for instance a protein comprising the entire amino acid sequence of any of the proteins depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96 and 98 can be used. Alternatively, a fragment of any of the proteins can be used.

As used herein, a cellular extract refers to a preparation or fraction which is made from a lysed or disrupted cell. The preferred source of cellular extracts will be cells derived from *Drosophila*, for instance, antennae and maxillary palp cellular extract.

A variety of methods can be used to obtain an extract of a cell. Cells can be disrupted using either physical or chemical disruption methods. Examples of physical disruption methods include, but are not limited to, sonication and mechanical shearing. Examples of chemical lysis methods include, but are not limited to, detergent lysis and enzyme lysis. A skilled artisan can readily adapt methods for preparing cellular extracts in order to obtain extracts for use in the present methods.

Once an extract of a cell is prepared, the extract is mixed with any of the proteins of the invention under conditions in which association of the protein with the binding partner can occur. A variety of conditions can be used, the most preferred being conditions that closely resemble conditions found in the cytoplasm of a *Drosophila* cell. Features such as osmolarity, pH, temperature, and the concentration of cellular extract used, can be varied to optimize the

association of the protein with the binding partner.

After mixing under appropriate conditions, the bound complex is separated from the mixture. A variety of techniques can be utilized to separate the mixture. For example, antibodies specific to a protein of the invention can be used to immunoprecipitate the binding partner complex. Alternatively, standard chemical separation techniques such as chromatography and density-sediment centrifugation can be used.

After removal of non-associated cellular constituents found in the extract, the binding partner can be dissociated from the complex using conventional methods. For example, dissociation can be accomplished by altering the salt concentration or pH of the mixture.

To aid in separating associated binding partner pairs from the mixed extract, the protein of the invention can be immobilized on a solid support. For example, the protein can be attached to a nitrocellulose matrix or acrylic beads. Attachment of the protein to a solid support aids in separating peptide-binding partner pairs from other constituents found in the extract. The identified binding partners can be either a single protein or a complex made up of two or more proteins. Alternatively, binding partners may be identified using a Far-Western assay according to the procedures of Takayama *et al.*, (1997) *Methods Mol. Biol.* 69, 171-184 or identified through the use of epitope tagged proteins or GST fusion proteins.

Alternatively, the nucleic acid molecules of the invention can be used in a yeast two-hybrid system. The yeast two-hybrid system has been used to identify other protein partner pairs (Alifragis *et al.*, (1997) *Proc. Natl. Acad. Sci. USA* 94, 13099-13104; Dong *et al.*, (1999) *Gene* 237, 421-428) and can readily be adapted to employ the nucleic acid molecules herein described.

In another embodiment, binding partners may be identified in insects using single unit recordings as previously described (Kaissling, (1995) *Single unit and electroantennogram recordings in insect olfactory organs*, in: Spielman & Brand (ed.) *Experimental Cell Biology of Taste and Olfaction*, CRC Press). Using single unit recordings *in vivo*, response profiles are established for potential ligands, these profiles are then categorized into distinct functional classes indicative of distinct receptor-ligand interactions (see, *e.g.*, U.S. Patent No. 5,993,778).

Single unit recordings in transgenic insects which contain transgenes resulting in over- or under-expression of a gene are also useful for identifying and characterizing ligands which bind to multiple olfactory receptors as well as identifying characterizing new olfactory receptors.

5 The nucleic acids of the invention and their corresponding proteins can be used on an array or microarray for high-throughput screening for agents which interact with either the nucleic acids of the invention or their corresponding proteins. An "array" or "microarray" generally refers to a grid system which has each position or probe cell occupied by a defined nucleic acid fragments also known as oligonucleotides. The arrays themselves are sometimes referred to as "chips" or "biochips". High-density nucleic acid and protein microarrays often
10 have thousands of probe cells in a variety of grid styles.

 A typical molecular detection chip includes a substrate on which an array of recognition sites, binding sites or hybridization sites are arranged. Each site has a respective molecular receptor which binds or hybridizes with a molecule having a predetermined
15 structure. The solid support substrates which can be used to form surface of the array or chip include organic and inorganic substrates, such as glass, polystyrenes, polyimides, silicon dioxide and silicon nitride. For direct attachment of probes to the electrodes, the electrode surface must be fabricated with materials capable of forming conjugates with the probes.

 Once the array is fabricated, a sample solution is applied to the molecular detection
20 chip and molecules in the sample bind or hybridize at one or more sites. The sites at which binding occurs are detected, and one or more molecular structures within the sample are subsequently deduced. Detection of labeled batches is a traditional detection strategy and includes radioisotope, fluorescent and biotin labels, but other options are available, including electronic signal transduction.

25 Polymer arrays of nucleic acid probes can be used to extract information from, for example, nucleic acid samples. These samples are exposed to the probes under conditions that permit binding. The arrays are then scanned to determine to which probes the sample molecules have interacted with the nucleic acids of the polymer array. One can obtain

information by careful probe selection and using algorithms to compare patterns of interactions. For example, the method is useful in screening for novel olfactory receptors in multiple organisms. For example, *Drosophila* degenerate olfactory receptor oligonucleotide arrays can be used to examine a nucleic acid sample from another insect species in order to
5 identify novel olfactory receptors in that species.

In typical applications, a complex solution containing one or more substances to be characterized contacts a polymer array comprising nucleic acids. For example, the array is comprised of nucleic acid probes. The probes of the array can be either DNA or RNA, which may be either single-stranded or double-stranded. In a preferred embodiment of the
10 invention, the probes are arranged (either by immobilization, typically by covalent attachment, of a pre-synthesized probe or by synthesis of the probe on the substrate) on the substrate or chips in lanes stretching across the chip and separated, and these lanes are in turned arranged in blocks of preferably five lanes, although blocks of other sizes will have useful application. The present invention provides individual probes, sets of probes, and
15 arrays of probe sets on chips, in specific patterns which are used to characterize the substances in a complex mixture by producing a distinct image which is representative of the binding interactions between the probes on the chip and the substances in the complex mixture. The pattern of hybridization to the chip allows inferences to be drawn about the substances present in the complex mixture.

The substances in the complex solution will bind to the nucleic acids on the array.
20 The substances of the complex mixture which bind to the nucleic acids of the array may include, but are not limited to, complementary nucleic acids, non-complementary nucleic acids, proteins, antibodies, oligosaccharides, etc. The types of binding may include, but are not limited to, specific and non-specific, competitive and non-competitive, allosteric,
25 cooperative, non-cooperative, complementary and non-complementary, etc. For example, the nucleic acids of the array can bind to complementary nucleic acids in the complex mixture but can also bind in a tertiary manner, independent of base pairing, to non-complementary nucleic acids.

The nucleic acids of the array or the substances of the complex mixture may be tagged with a detectable label. The detectable label can be, for example, a luminescent label, a light scattering label or a radioactive label. Accordingly, locations at which substances interact can be identified by either determining if the signal of the label has been quenched by binding or
5 identifying locations where the signal of the label is present in cases where the substances of the complex mixture have been labeled. Based on the locations where binding is detected, information regarding the complex mixture can be obtained.

The methods of this invention will find particular use wherever high through-put of samples is required. In particular, this invention is useful in ligand screening settings and for
10 determining the composition of complex mixtures.

Polypeptides are an exemplary system for exploring the relationship between structure and function in biology. When the twenty naturally occurring amino acids are condensed into a polymeric molecule they form a wide variety of three-dimensional configurations, each resulting from a particular amino acid sequence and solvent condition. For example, the
15 number of possible polypeptide configurations using the twenty naturally occurring amino acids for a polymer five amino acids long is over three million. Typical proteins are more than one-hundred amino acids in length.

In typical applications, a complex solution containing one or more substances to be characterized contacts a polymer array comprising polypeptides. The polypeptides of the
20 invention can be prepared by classical methods known in the art, for example, by using standard solid phase techniques. The standard methods include exclusive solid phase synthesis, partial solid phase synthesis methods, fragment condensation, classical solution synthesis and recombinant DNA technology (see Merrifield, (1963) Am. Chem. Soc. 85, 2149-2152). On solid phase, the synthesis is typically commenced from the C-terminal end of
25 the peptide using an alpha-amino protected resin. A suitable starting material can be prepared, for instance, by attaching the required alpha-amino acid to a chloromethylated resin, a hydroxy-methyl resin or a benzhydrylamine resin.

The alpha-amino protecting groups are those known to be useful in the art of stepwise

synthesis of peptides. Included are acyl type protecting groups, aromatic urethane type protecting groups, aliphatic urethane protecting groups and alkyl type protecting groups. The side chain protecting group remains intact during coupling and is not split off during the deprotection of the amino-terminus protecting group or during coupling. The side chain protecting group must be removable upon the completion of the synthesis of the final peptide and under reaction conditions that will not alter the target peptide.

After removal of the alpha-amino protecting group, the remaining protected amino acids are coupled stepwise in the desired order. An excess of each protected amino acid is generally used with an appropriate carboxyl group activator such as dicyclohexylcarbodiimide (DCC) in solution, for example, in methylene chloride, dimethyl formamide (DMF) mixtures.

These procedures can also be used to synthesize peptides in which amino acids other than the twenty naturally occurring, genetically encoded amino acids are substituted at one, two, or more positions of any of the compounds of the invention. For instance, naphthylalanine can be substituted for tryptophan, facilitating synthesis. Other synthetic amino acids that can be substituted into the peptides of the present invention include L-hydroxypropyl, L-3, 4-dihydroxyphenylalanyl, d-amino acids such as L-d-hydroxylysyl and D-d-methylalanyl, L- α -methylalanyl and β -amino acids non-naturally occurring synthetic amino acids can also be incorporated into the peptides of the present invention (see Roberts *et al.*, (1983) Peptide Synthesis 5, 341-449).

One can replace the naturally occurring side chains of the twenty genetically encoded amino acids (or D amino acids) with other side chains, for instance with groups such as alkyl, lower alkyl, cyclic four, five, six, to seven-membered alkyl, amide, amide lower alkyl, amide di(lower alkyl), lower alkoxy, hydroxy, carboxy and the lower ester derivatives thereof, and with four, five, six, to seven-membered heterocyclic. In particular, proline analogs in which the ring size of the proline residue is changed from five members to four, six or seven members can be employed. Cyclic groups can be saturated or unsaturated, and if unsaturated, can be aromatic or non-aromatic. Heterocyclic groups preferably contain one or more

nitrogen, oxygen, and/or sulphur heteroatoms. Examples of such groups include the furazanyl, furyl, imidazolidinyl, imidazolyl, imidazolinyl, isothiazolyl, isoxazolyl, morpholinyl, oxazolyl, piperazinyl, piperidyl, pyranyl, pyrazinyl, pyrazolidinyl, pyrazolinyl, pyrazolyl, pyridazinyl, pyridyl, pyrimidinyl, pyrrolidinyl, pyrrolinyl, pyrrolyl, thiadiazolyl, thiazolyl, thienyl, thiomorpholinyl and triazolyl. These heterocyclic groups can be substituted or unsubstituted. Where a group is substituted, the substituent can be alkyl, alkoxy, halogen, oxygen, or substituted or unsubstituted phenyl.

One can also readily modify the peptides of the instant invention by phosphorylation (see Bannwarth *et al.*, (1996) Biorg. Med. Chem. Let. 6, 2141-2146) and other methods for making peptide derivatives of the compounds of the present invention are described in Hruby *et al.*, (1990) Biochem. J. 268, 249-262). Thus, the peptide compounds of the invention also serve as a basis to prepare peptide mimetics with similar biological activity. The array can also comprise peptide mimetics with the same or similar desired biological activity as the corresponding peptide compound but with more favorable activity than the peptide with respect to solubility, stability, and susceptibility to hydrolysis and proteolysis (see Morgan *et al.*, (1989) Ann. Rep. Med. Chem. 24, 243-252).

Peptides suitable for use in this embodiment generally include those peptides, for example, ligands, that bind to a receptor, such as seven transmembrane proteins. Such peptides typically comprise about 150 amino acid residues or less and, more preferably, about 100 amino acid residues or less.

The peptides of the present invention may exist in a cyclized form with an intramolecular disulfide bond between the thiol groups of the cysteines. Alternatively, an intermolecular disulfide bond between the thiol groups of the cysteines can be produced to yield a dimeric (or higher oligomeric) compound. One or more of the cysteine residues may also be substituted with a homocysteine. Other embodiments of this invention provide for analogs of these disulfide derivatives in which one of the sulfurs has been replaced by a CH₂ group or other isostere for sulfur. These analogs can be made via an intramolecular or intermolecular displacement, using methods known in the art.

H. Methods to Identify Agents that Modulate Expression of DORs.

Another embodiment of the present invention provides methods for identifying agents that modulate the expression of a nucleic acid encoding any one of the DOR proteins of the invention such as any protein having the amino acid sequence depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96 and 98. Such assays may utilize any available means of monitoring for changes in the expression level of the nucleic acids of the invention. As used herein, an agent is said to modulate the expression of a nucleic acid of the invention, for instance a nucleic acid encoding any one of the proteins having the amino acid sequence depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96 and 98, if it is capable of up- or down-regulating expression of the nucleic acid in a cell.

In one assay format, cell lines that contain reporter gene fusions between the open reading frame of any one of the nucleotides depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95 and 97 and any assay fusion partner may be prepared. Numerous assay fusion partners are known and readily available including the firefly luciferase gene and the gene encoding chloramphenicol acetyltransferase (Alam *et al.*, (1990) Anal. Biochem. 188, 245-254). Cell lines containing the reporter gene fusions are then exposed to the agent to be tested under appropriate conditions and time. Differential expression of the reporter gene between samples exposed to the agent and control samples identifies agents which modulate the expression of a nucleic acid encoding at least one of the proteins having the sequence depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96 and 98.

Additional assay formats may be used to monitor the ability of the agent to modulate the expression of a nucleic acid encoding at least one protein of the invention selected from

the group of proteins having SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96 and 98. For instance, mRNA expression may be monitored directly by hybridization to the nucleic acids of the invention. Cell lines are exposed to the agent to be tested under appropriate conditions and time and total RNA or mRNA is isolated by standard procedures such those disclosed in Sambrook *et al.*, (1985) Molecular Cloning - A Laboratory Manual, Cold Spring Harbor Laboratory Press.

Probes to detect differences in RNA expression levels between cells exposed to the agent and control cells may be prepared from the nucleic acids of the invention. It is preferable, but not necessary, to design probes which hybridize only with target nucleic acids under conditions of high stringency. Only highly complementary nucleic acid hybrids form under conditions of high stringency. Accordingly, the stringency of the assay conditions determines the amount of complementary nucleotides which should exist between two nucleic acid strands in order to form a hybrid. Stringency should be chosen to maximize the difference in stability between the probe:target hybrid and potential probe:non-target hybrids.

Probes may be designed from the nucleic acids of the invention through methods known in the art. For instance, the G+C content of the probe and the probe length can affect probe binding to its target sequence. Methods to optimize probe specificity are commonly available in Sambrook *et al.*, (1985) Molecular Cloning - A Laboratory Manual, Cold Spring Harbor Laboratory Press; or Ausubel *et al.*, (1995) Current Protocols in Molecular Biology, Greene Publishing Company.

Hybridization conditions are modified using known methods, such as those described by Sambrook *et al.*, (1985) and Ausubel *et al.*, (1995) as required for each probe.

Hybridization of total cellular RNA or RNA enriched for polyA⁺ RNA can be accomplished in any available format. For instance, total cellular RNA or RNA enriched for polyA RNA can be affixed to a solid support and the solid support exposed to at least one probe comprising at least one, or part of one of the sequences of the invention under conditions in which the probe will specifically hybridize. Alternatively, nucleic acid fragments comprising

at least one, or part of one of the sequences of the invention can be affixed to a solid support, such as a porous glass wafer. The glass wafer can then be exposed to total cellular RNA or polyA RNA from a sample under conditions in which the affixed sequences will specifically hybridize. Such glass wafers and hybridization methods are widely available, for example, those disclosed by Beattie (WO 95/11755). By examining for the ability of a given probe to specifically hybridize to an RNA sample from an untreated cell population and from a cell population exposed to the agent, agents which up- or down-regulate the expression of a nucleic acid encoding at least one protein having the amino acid sequence depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96 and 98 are identified.

Hybridization for qualitative and quantitative analysis of mRNA may also be carried out by using a RNase Protection Assay (*i.e.*, RPA, see Ma *et al.*, (1996) Methods 10, 273-238). Briefly, an expression vehicle comprising cDNA encoding the gene product and a phage specific DNA dependent RNA polymerase promoter (*e.g.*, T7, T3 or SP6 RNA polymerase) is linearized at the 3' end of the cDNA molecule, downstream from the phage promoter, wherein such a linearized molecule is subsequently used as a template for synthesis of a labeled antisense transcript of the cDNA by *in vitro* transcription. The labeled transcript is then hybridized to a mixture of isolated RNA (*i.e.*, total or fractionated mRNA) by incubation at 45°C overnight in a buffer comprising 80% formamide, 40 mM Pipes, pH 6.4, 0.4 M NaCl and 1 mM EDTA. The resulting hybrids are then digested in a buffer comprising 40 µg/ml ribonuclease A and 2 µg/ml ribonuclease. After deactivation and extraction of extraneous proteins, the samples are loaded onto urea-polyacrylamide gels for analysis.

In another assay format, agents which effect the expression of the instant gene products, cells or cell lines would first be identified which express said gene products physiologically. Cells and cell lines so identified would be expected to comprise the necessary cellular machinery such that the fidelity of modulation of the transcriptional apparatus is maintained with regard to exogenous contact of agent with appropriate surface

transduction mechanisms and the cytosolic cascades. Further, such cells or cell lines would be transduced or transfected with an expression vehicle (e.g., a plasmid or viral vector) construct comprising an operable non-translated 5'-promoter containing end of the structural gene encoding the instant gene products fused to one or more antigenic fragments, which are peculiar to the instant gene products, wherein said fragments are under the transcriptional control of said promoter and are expressed as polypeptides whose molecular weight can be distinguished from the naturally occurring polypeptides or may further comprise an immunologically distinct tag. Such a process is well known in the art (see Maniatis *et al.*, (1982) Molecular Cloning - A Laboratory Manual, Cold Spring Harbor Laboratory Press).

Cells or cell lines transduced or transfected as outlined above would then be contacted with agents under appropriate conditions; for example, the agent comprises an acceptable excipient and is contacted with cells comprised in an aqueous physiological buffer such as phosphate buffered saline (PBS) at physiological pH, Eagles balanced salt solution (BSS) at physiological pH, PBS or BSS comprising serum or conditioned media comprising PBS or BSS and/or serum incubated at 37°C. Said conditions may be modulated as deemed necessary by one of skill in the art. Subsequent to contacting the cells with the agent, said cells will be disrupted and the polypeptides from disrupted cells are fractionated such that a polypeptide fraction is pooled and contacted with an antibody to be further processed by immunological assay (e.g., ELISA, immunoprecipitation or Western blot). The pool of proteins isolated from the "agent contacted" sample will be compared with a control sample where only the excipient is contacted with the cells and an increase or decrease in the immunologically generated signal from the "agent contacted" sample compared to the control will be used to distinguish the effectiveness of the agent.

I. Methods to Identify Agents that Modulate Activity of DORs

Another embodiment of the present invention provides methods for identifying agents that modulate at least one activity of a protein of the invention such as any one of the proteins having the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26,

28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96 and 98. Such methods or assays may utilize any means of monitoring or detecting the desired activity.

In one format, the relative amounts of a protein of the invention between a cell
5 population that has been exposed to the agent to be tested compared to an un-exposed control cell population may be assayed. In this format, probes such as specific antibodies are used to monitor the differential expression of the protein in the different cell populations. Cell lines or populations are exposed to the agent to be tested under appropriate conditions and time. Cellular lysates may be prepared from the exposed cell line or population and a control,
10 unexposed cell line or population. The cellular lysates are then analyzed with the probe.

Antibody probes are prepared by immunizing suitable mammalian hosts in appropriate immunization protocols using the peptides, polypeptides or proteins of the invention if they are of sufficient length, or if desired, required to enhance immunogenicity, conjugated to suitable carriers. Methods for preparing immunogenic conjugates with carriers such as BSA,
15 KLH, or other carrier proteins are well known in the art. In some circumstances, direct conjugation using, for example, carbodiimide reagents may be effective; in other instances linking reagents such as those supplied by Pierce Chemical Co., may be desirable to provide accessibility to the hapten. The hapten peptides can be extended at either the amino or carboxy terminus with a cysteine residue or interspersed with cysteine residues, for example,
20 to facilitate linking to a carrier. Administration of the immunogens is conducted generally by injection over a suitable time period and with use of suitable adjuvants, as is generally understood in the art. During the immunization schedule, titers of antibodies are taken to determine adequacy of antibody formation.

While the polyclonal antisera produced in this way may be satisfactory for some
25 applications, for some applications, use of monoclonal preparations is preferred. Immortalized cell lines which secrete the desired monoclonal antibodies may be prepared using the standard method of Kohler & Milstein, (1975) Nature 256, 495-497 or modifications which effect immortalization of lymphocytes or spleen cells, as is generally known. The

immortalized cell lines secreting the desired antibodies are screened by immunoassay in which the antigen is the peptide hapten, polypeptide or protein. When the appropriate immortalized cell culture secreting the desired antibody is identified, the cells can be cultured either *in vitro* or by production in ascites fluid.

5 The desired monoclonal antibodies are then recovered from the culture supernatant or from the ascites supernatant. Fragments of the monoclonal or polyclonal antisera which contain the immunologically significant portion can be used as antagonists, as well as the intact antibodies. Use of immunologically reactive fragments, such as the Fab, Fab' of F(ab')₂ fragments is often preferable, as these fragments are generally less immunogenic than the
10 whole immunoglobulin.

 The antibodies or fragments may also be produced, using current technology, by recombinant means. Antibody regions that bind specifically to the desired regions of the protein can also be produced in the context of chimeras with multiple species origin, particularly humanized antibodies.

15 Agents that are assayed in the above method can be randomly selected or rationally selected or designed. As used herein, an agent is said to be randomly selected when the agent is chosen randomly without considering the specific sequences involved in the association of the a protein of the invention alone or with its associated substrates, binding partners, etc. An example of randomly selected agents is the use a chemical library or a peptide combinatorial
20 library, or a growth broth of an organism.

 As used herein, an agent is said to be rationally selected or designed when the agent is chosen on a non-random basis which takes into account the sequence of the target site and its conformation in connection with the agent's action. Agents can be rationally selected or rationally designed by utilizing the peptide sequences to identify proposed binding motifs,
25 glycosylation and phosphorylation sites on the protein.

 The agents of the present invention can be, as examples, peptides, small molecules, vitamin derivatives, as well as carbohydrates. A skilled artisan can readily recognize that there is no limit as to the structural nature of the agents of the present invention. Dominant-

negative proteins, DNA encoding these proteins, antibodies to these proteins, peptide fragments of these proteins or mimics of these proteins may be contacted with cells to affect function. "Mimic" as used herein refers to the modification of a region or several regions of a peptide molecule to provide a structure chemically different from the parent peptide but topographically and functionally similar to the parent peptide (see Meyers, (1995) Molecular Biology & Biotechnology, VCH Publishers).

The peptide agents of the invention can be prepared using standard solid phase (or solution phase) peptide synthesis methods, as is known in the art. In addition, the DNA encoding these peptides may be synthesized using commercially available oligonucleotide synthesis instrumentation and produced recombinantly using standard recombinant production systems. The production using solid phase peptide synthesis is necessitated if non-gene-encoded amino acids are to be included.

Another class of agents of the present invention are antibodies immunoreactive with critical positions of proteins of the invention. Antibody agents are obtained by immunization of suitable mammalian subjects with peptides, containing as antigenic regions, those portions of the protein intended to be targeted by the antibodies.

J. Transgenic Organisms

Transgenic insects containing mutant, knock-out or modified genes corresponding to any one of the cDNA sequences depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95 and 97 are also included in the invention.

Transgenic insects are genetically modified insects into which recombinant, exogenous or cloned genetic material has been experimentally transferred. Such genetic material is often referred to as a "transgene". The nucleic acid sequence of the transgene, in this case a form of any one of the sequences depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95 and 97, may be integrated either at a locus of a genome

where that particular nucleic acid sequence is not otherwise normally found or at the normal locus for the transgene. The transgene may consist of nucleic acid sequences derived from the genome of the same species or of a different species than the species of the target insect.

5 The term "germ cell line transgenic insect" refers to a transgenic insect in which the genetic alteration or genetic information was introduced into a germ line cell, thereby conferring the ability of the transgenic insect to transfer the genetic information to offspring. If such offspring in fact possess some or all of that alteration or genetic information, then they too are transgenic insects.

10 The alteration or genetic information may be foreign to the species of insect to which the recipient belongs, foreign only to the particular individual recipient, or may be genetic information already possessed by the recipient. In the last case, the altered or introduced gene may be expressed (*i.e.*, over-expression and knock-out) differently than the native gene.

15 Transgenic insects can be produced by a variety of different methods including P element-mediated transformation by microinjection (see, *e.g.*, Rubin & Spradling, (1982) Science 218, 348-353; Orr & Sohal, (1993) Arch. Biochem. Biophys. 301, 34-40), transformation by microinjection followed by transgene mobilization (Mockett *et al.*, (1999) Arch. Biochem. Biophys. 371, 260-269), electroporation (Huynh & Zieler, (1999) J. Mol. Biol. 288, 13-20) and through the use of baculovirus (Yamao *et al.*, (1999) Genes Dev. 13, 511-516. Furthermore, the use of adenoviral vectors to direct expression of a foreign gene to
20 olfactory neuronal cells can also be used to generate transgenic insects (see, *e.g.*, Holtmaat *et al.*, (1996) Brain. Res. Mol. Brain Res. 41, 148-156).

A number of recombinant or transgenic insects have been produced, including those which over-express superoxide dismutase (Mockett *et al.*, (1999) Arch. Biochem. Biophys. 371, 260-269); express Syrian hamster prion protein (Raeber *et al.*, (1995) Mech. Dev. 51,
25 317-327); express cell-cycle inhibitory peptide aptamers (Kolonin & Finley (1998) Proc. Natl. Acad. Sci. USA 95, 14266-14271); and those which lack expression of the putative ribosomal protein S3A gene (Reynaud *et al.*, (1997) Mol. Gen. Genet. 256, 462-467).

While insects remain the preferred choice for most transgenic experimentation, in

some instances it is preferable or even necessary to use alternative animal species.

Transgenic procedures have been successfully utilized in a variety of animals, including mice, rats, sheep, goats, pigs, dogs, cats, monkeys, chimpanzees, hamsters, rabbits, cows and guinea pigs (see, e.g., Kim *et al.*, (1997) Mol. Reprod. Dev. 46, 515-526; Houdebine, (1995)

5 Reprod. Nutr. Dev. 35, 609-617; Petters, (1994) Reprod. Fertil. Dev. 6, 643-645; Schnieke *et al.*, (1997) Science 278, 2130-2133; and Amoah, (1997) J. Anim. Sci. 75, 578-585).

The method of introduction of nucleic acid fragments into insect cells can be by any method which favors co-transformation of multiple nucleic acid molecules. For instance, *Drosophila* embryonic Schneider line 2 (S2) cells can be stably transfected as previously
10 described (Schneider, (1972) J. Embryol. Exp. Morphol. 27, 353-365). Detailed procedures for producing transgenic insects are readily available to one skilled in the art (see Rubin & Spradling, (1982) Science 218, 348-353; Orr & Sohal, (1993) Arch. Biochem. Biophys. 301, 34-40, herein incorporated by reference in their entirety).

15 **K. Uses for Agents that Modulate at Least One Activity of DORs**

1. Introduction.

Organisms, including insects, are continually exposed to a great number of volatiles released by other organisms as well as by other aspects of their environment. The olfactory receptor genes of the present invention play an important role in the detection and processing
20 of these chemical stimuli, some of which have been implicated in initiating and modulating host-seeking and other behaviors, such as mating behaviors (see, for example, Roth, (1951) Ann. Entomol. Soc. Am. 44, 59-74; Jones *et al.*, (1976) Ent. Exp. Appn. 19, 19-22; Gillies, (1980) Bull. Ent. Res. 70, 525-532; Kline *et al.*, (1991) J. Med. Entomol. 28, 254-258). For a recent, thorough review of the many practical applications of the present invention (see Karg
25 & Suckling, (1999) Applied aspects of insect olfaction, in: Hansson (ed.), Insect Olfaction, Springer, which is incorporated by reference in its entirety).

Most importantly, the DOR genes of the present invention may be used to track down odor receptor genes in insects that damage crops or transmit diseases. The present invention

provides the tools and methodologies for finding specific compounds that interfere with the insects' ability to detect odors.

Of course, the present invention has important implications for improved methods of using pheromones and other semiochemicals for pest control. In addition, recent
5 advancements in many other fields have greatly increased the variety of additional technologies for which the present invention also has significant applications. Examples of such advancements include, but are not limited to the following: i) the development and application of new techniques of chemical identification and synthesis; ii) new chemical release techniques; iii) more sophisticated application technologies; and iv) more detailed
10 information about the behavior of specific organisms.

While not wishing to be bound by the specific embodiments discussed herein, the following sections provide an overview of the wide variety of applications for which the present invention may be employed.

2. Definitions.

15 As used herein, the term "allomones" refers to any chemical substance produced or acquired by an organism that, when it contacts an individual of another species, evokes in the receiver a behavioral or developmental reaction adaptively favorable to the transmitter.

As used herein, the term "host" refers to any organism on which another organism depends for some life function. Examples of hosts include, but are not limited to, humans
20 which may serve as a host for the feeding of certain species of mosquito and the leaves of soybeans (*Glycine max*(L.)) which may act as hosts for the oviposit of the green cloverworm (*Plathypena scabra* (F.)).

As used herein, the term "kairomones" refers to any of a heterogeneous group of chemical messengers that are emitted by organisms of one species but benefit members of
25 another species. Examples include, but are not limited to, attractants, phagostimulants, and other substances that mediate the positive responses of, for example, predators to their prey, herbivores to their food plants, and parasites to their hosts. Kairomones suitable for the purposes of the invention and methods of obtaining them are described, for example, Science

(1966) 154, 1392-93; Hedin, (1985) Bioregulators for Pest Control, American Chemical Society, Washington, 353-366.

As used herein, the term "pheromone" refers to a substance, or characteristic mixture of substances, that is secreted and released by an organism and detected by a second organism of the same or a closely related species, in which it causes a specific reaction, such as a definite behavioral reaction or a developmental process. Examples include, but are not limited to, the mating pheromones of fungi and insects. More than a thousand moth sex pheromones (Toth *et al.*, (1992) J. Chem. Ecol. 18, 13-25 ; Arn *et al.*, (1998) Appl. Entomol. Zoo. 33, 507-511) and hundreds of other pheromones have now been identified, including aggregation pheromones from beetles and other groups of insects. Various compositions, including resins and composite polymer dispensers, have been developed for the controlled release of pheromones have been developed (see, *e.g.*, U.S. Patent No. 5,750,129 & 5,504,142).

As used herein, the term "semiochemical" refers to any chemical substance that delivers a message or signal from one organism to another. Examples of such chemicals include, but are not limited to, pheromones, kairomones, oviposition deterrents, or stimulants, and a wide range of other classes of chemicals (see, for example, Nordlund, (1981) Semiochemicals: A review of the terminology, in: Nordlund *et al.*, (ed.) Semiochemicals: Their Role in Pest Control, John Wiley; Howse *et al.*, (1998) Insect Pheromones and Their Use in Pest Management, Chapman & Hall, London).

As used herein, the term "synomones" refers to any chemical substance which benefits both the emitter and receiver. Examples include, but are not limited to, compounds involved in floral attraction of pollinators and species-isolating mechanisms, such as sex pheromones of related species, where an inhibitor often functions to prevent mating among sympatric species.

As used herein, the term "volatile" refers to a chemical which evaporates readily at those temperatures and pressures which are considered the relevant temperatures and pressures for the reference organism of interest.

3. As Tools for Further Scientific Research.

Identification of Olfactory Receptor Genes in Other Organisms. The algorithms of the

present invention may be used directly to search for olfactory receptor genes in other organisms, as explained elsewhere herein.

Alternatively, nucleic acid probes or primers may be designed based on the DOR genes of the present invention. Such probes or primers may be used to identify and isolate olfactory receptor genes in other organisms. Methods of creating and using the necessary nucleic acid probes and primers are discussed elsewhere herein.

The highest probability of success in locating olfactory genes in other organisms using the DOR genes of the present invention will most likely occur by using a boot-strapping or leap-frogging method. Such methods involve first probing organisms most related to fruit flies and successively progressing to more unrelated organisms, using the most newly identified olfactory receptor genes to identify similar genes in the next, more unrelated, insect of interest. Thus, the first organisms to probe with the DOR genes of the present invention most preferably may be other flies from the order *Diptera* (i.e., the two-winged or true flies). Examples of suitable flies include, but are not limited to, the tsetse fly, horse fly, house fly, bluebottle fly, hover fly and mosquito. *Dipterans* which transmit diseases causing serious health problems are of particular interest (e.g., horse fly, tsetse fly, mosquito).

After the identification of olfactory receptor genes in various *Diptera* insects, the next organisms to probe most preferably may be from orders within the same subclass as *Diptera*. Finally, the next insects to use would be those from orders not within the same subclass as *Diptera*.

The insects which cause substantial health risks, crop damage, or other significant damage (e.g., to housing structure or cotton clothing) may be the most desirable targets for such studies. Examples of such insects include, but are not limited to, green cloverworm, Mexican bean beetle, potato leafhopper, corn earworm, green stink bug, northern corn rootworm, western corn rootworm, cutworms, wireworms, thrips, fleas, aphids (e.g., pea aphid, spotted alfalfa aphid), European corn borer, fall armyworm, southwestern corn borer, grasshoppers, Japanese beetle, termites, leafhoppers (e.g., potato leafhopper, three-cornered alfalfa hopper), stink bugs, crickets, Hessian fly, greenbugs and weevils (e.g., alfalfa weevil,

bollweevil).

Olfactory receptor genes identified by this process may then be used to screen non-Insecta organisms for olfactory receptor genes. Organisms of interest may include, but be limited to, mites, ticks, spiders, nematodes, centipedes, mice, rats, salmon, pigeons, dogs,
5 horses and humans.

Genetic Manipulations. The tools and methodologies of the present invention may be used by neurobiologists to probe more complex workings of an organism's response system, including those of a mammal's brain.

Knock-outs. By systematically knocking out the olfactory receptor genes of the
10 present invention and observing the effects on odor sensitivity and behavior, researchers will be able to piece together a wiring diagram of the olfactory system of the fruit fly.

The term "knock-out" generally refers to mutant organisms which contain a null allele of a specific gene. Methods of making knock-out or disruption transgenic animals, especially mice, are generally known by those skilled in the art and are discussed herein and elsewhere
15 (see, for example, the section herein entitled Transgenic Organisms and the following: Manipulating the Mouse Embryo, (1986) Cold Spring Harbor Laboratory Press; Capecchi, (1989) Science 244, 1288-1292; Li *et al.*, (1995) Cell 80, 401-411; U.S. Patent No. 5,981,830 & 5,789,654, each of which is incorporated herein by reference.

Parallel studies may be conducted in other organisms by using the olfactory receptor
20 genes and the methods of the present invention to identify the olfactory receptor genes of other organisms and then creating knock-outs for the olfactory receptor genes of those organisms.

Disabling Genes. Using the olfactory receptor genes of the present invention, it is now possible to selectively disable specific DOR genes and look for changes in odor response and
25 behavior. Parallel studies may be conducted in other organisms by using the olfactory receptor genes and the methods of the present invention to identify the olfactory receptor genes of other organisms and then disabling olfactory receptor genes of those organisms.

Methods of disabling genes are generally known by those skilled in the art. An

example of an effective disabling modification would be a single nucleotide deletion occurring at the beginning of an olfactory receptor gene that would produce a translational reading frameshift. Such a frameshift would disable the gene, resulting in non-expressible gene product and thereby disrupting functional protein production by that gene. Protease production by the gene could be disrupted if the regulatory regions or the coding regions of the protease genes are disrupted.

In addition to disabling genes by deleting nucleotides, causing a transitional reading frameshift, disabling modifications would also be possible by other techniques including insertions, substitutions, inversions or transversions of nucleotides within the gene's DNA that would effectively prevent the formation of the protein coded for by the DNA.

It is also within the capabilities of one skilled in the art to disable genes by the use of less specific methods. Examples of less specific methods would be the use of chemical mutagens such as hydroxylamine or nitrosoguanidine or the use of radiation mutagens such as gamma radiation or ultraviolet radiation to randomly mutate genes, such as the DOR genes of the present invention. Such mutated strains could, by chance, contain disabled olfactory receptor genes such that the genes are no longer capable of producing functional proteins for any one or more of the domains. The presence of the desired disabled genes could be detected by routine screening techniques. For further guidance, see U.S. Patent No. 5,759,538.

Over-expression. Using the olfactory receptor genes of the present invention, it is now possible to selectively over-express specific DOR genes and look for changes in odor response and behavior. Parallel studies may be conducted in other organisms by using the olfactory receptor genes and the methods of the present invention to identify the olfactory receptor genes of other organisms and then overexpress the olfactory receptor genes of those organisms.

Methods of overexpressing genes are generally known by those skilled in the art. For examples of producing cells which overexpress specific genes, see, for example, U.S. Patent Numbers 5,905,146; 5,849,999; 5,859,311; 5,602,309; 5,952,169 and 5,772,997 (HER2 receptor).

Modulating or Inhibiting Expression. Using the olfactory receptor genes of the present invention, it is now possible to selectively modulate or inhibit specific DOR genes using antisense oligomers which specifically hybridize with the DNA or RNA encoding the DOR genes. One skilled in the art could so modulate or inhibit the expression of the DOR genes and detect for changes in odor response and behavior. Parallel studies may be conducted in other organisms by using the olfactory receptor genes and the methods of the present invention to identify the olfactory receptor genes in other organisms and then use antisense oligers to the olfactory receptor genes of those organisms. Methods for inhibiting expression of genes, especially genes coding for receptor genes, using antisense constructs, including generation of antisense sequences *in situ* are described, for example, in U.S. Patent Numbers 5,856,099; 5,556,956; 5,716,846; 5,135,917 and 6,004,814.

Other methods that can be used to inhibit expression of an endogenous gene are applicable to the present invention. For example, formation of a triple helix at an essential region of a duplex gene serves this purpose. The triplex code, permitting design of the proper single stranded participant is also known in the art. (See H. E. Moser, *et al.*, (1987) Science 238: 645-650 and M. Cooney, *et al.*, (1988) Science 241: 456-459). Regions in the control sequences containing stretches of purine bases are particularly attractive targets. Triple helix formation along with photocrosslinking is described, *e.g.*, in Praseuth *et al.*, (1988) Proc. Natl Acad. Sci. USA 85:1349-1353.

Studying Behavior. The present invention is useful for studying the developmental aspects of the olfactory receptor genes which appear to be active at different times during development. Such studies may help organize the olfactory systems in various organisms and may help explain the behavior of various organisms.

The tools and methodologies of the present invention may be used to study the influence of environmental conditions on pheromone communication. For example, newly identified olfactory receptor genes may be used to study the effects of different rearing temperatures and light regimes (selected to mimic those occurring in the spring and summer growing seasons) on the response of various *Lepidoptera* insects, such as the cabbage looper

moth (*Trichoplusia ni* (Hubner)). For a description of the methods which might be used for such a study, see, for example, Grant *et al.*, (1996) *Physiol. Entomol.* 21, 59-63.

4. For Organism Detection, Monitoring and Control.

General Pest Management. The olfactory receptor genes identified herein and
5 identified using the methods of the present invention may be used to identify compounds which may be used for pest management. It is especially desirable to utilize various aspects of the present invention for pest management related to crop protection.

The application of pheromones is now firmly established as a key component of pest management and control, especially within the framework of integrated pest management
10 (IPM). An object of organism control is to modulate an organism's behavior or activity so as to reduce the irritation, sickness, or death of the host (*e.g.*, a plant host), or to decrease the general health and proliferation of the organism.

For example, the propagation of a mouse population in a given area of actual or potential mice infestation may be prevented or inhibited by treating such an area with an
15 effective amount of male mouse pheromones, wherein such pheromones have male mouse aversion signaling properties (see, *e.g.*, U.S. Patent No. 5,252,326).

Insect Repellents and Insecticides. The present invention provides the tools and methodologies useful for identifying compounds which modulate insect behavior by exploiting the sensory capabilities of the target insect. For example, attempts have been made
20 to describe and synthesize the complex interactions which underlie host-seeking behavior in mosquitoes. Using the methods and olfactory receptor genes of the present invention, it is possible to design specific compounds which target mosquito olfactory receptor genes. Thus, the present invention provides the ability to alter or to eliminate the orientation and feeding behaviors of mosquitoes and thereby have a positive impact on world health by controlling
25 mosquito-borne diseases, such as malaria.

Mosquito olfactory receptor genes may be identified and/or targeted using various aspects of the present invention. For example, the olfactory receptor genes of the present invention may be used to design probes as discussed elsewhere herein for the identification

and characterization of mosquito olfactory receptor genes. Alternatively, the algorithm of the present invention may be used to identify mosquito olfactory receptor genes in the genetic databases for mosquitoes. Once the mosquito olfactory receptor genes are identified, then various screening methods described elsewhere herein, such as the high throughput assays discussed elsewhere herein, may be used to identify synthetic and natural compounds which may modulate the behavior of the insect.

Mating Enhancement and Disruption. The olfactory receptor genes identified herein and identified using the methods of the present invention may be used to identify compounds which interfere with the orientation and mating of a wide range of organisms, including insects. Thus, the present invention enables the identification of compositions which disrupt insect mating by selective inhibition of specific receptor genes involved in mating attraction (see, *e.g.*, U.S. Patent No. 5,064,820).

Animal Repellants. The olfactory receptor genes identified herein and identified using the methods of the present invention may be used to identify compounds which may be used as animal repellants. Such compositions may be used to repel both predatory and non-predatory animals (see, *e.g.*, U.S. Patent No. 4,668,455).

6. Organism Attraction.

Insect Attractants. The olfactory receptor genes identified herein and identified using the methods of the present invention may be used to identify compounds which attract specific insects to a particular location (see, *e.g.*, U.S. Patent No. 4,880,624 & 4,851,218).

For example, aspects of the present invention may be used in various methods which reduce or eliminate the levels of particular insect pests, such as mosquitoes and tsetse flies. As a particular example, insect traps can be created wherein the pheromone attracts a particular insect, like the tsetse fly, and the insect so attracted dies in the trap. In this way, the population of tsetse flies may be reduced or eliminated in a particular area.

The insect attractant compositions so identified may also be combined with an insecticide, for example as an insect bait in microencapsulated form. Alternatively, or in addition, the insect attractant composition may be placed inside an insect trap, or in the

vicinity of the entrance to an insect trap.

In addition to killing insects, the trapping of insects is often very important for estimating or calculating how many insects of a particular type are feeding within a specific area. Such estimates are used to determine where and when insecticide spraying should be commenced and terminated.

Insect traps which may be used are, for example, those as described in PCT/BG93/01442 and U.S. Patent No. 5,713,153. Specific examples of insect traps include, but are not limited to, the Gypsy Moth Delta Trap®, Boll Weevil Scout Trap®, Jackson trap, Japanese beetle trap, McPhail trap, Pherocon 1C trap, Pherocon II trap, Pherocon AM trap and Trogo trap.

Kairomones may be used as an attractancy for the enhancement of the pollination of selected plant species.

Attractant compositions which demonstrate biological activity toward one sex which is greater than toward the opposite sex may be useful in trapping one sex of a specific organism over another. For example, a composition may be a highly effective attractant for male apple ermine moths (*Yponomeuta malinellus* (Zeller)) and not so effective an attractant for female apple ermine moths. By attracting adult males to field traps, the composition provides a means for detecting, monitoring, and controlling this agricultural pest (see, e.g., U.S. Patent No. 5,380,524).

Attracting Predators and Parasitoids. The olfactory receptor genes of the present invention and the olfactory receptor genes identified using the methods of the present invention may also be used to identify chemicals which attract various predators and parasitoids. Attracting the predators and parasitoids which attack certain pests offers an alternative method of pest management.

Animal Attractants. The olfactory receptor genes identified herein and those identified by the methods of the present invention may be used to identify chemicals which attract household domesticated animals. For example, a pheromone-containing litter preparation may attract the animals and absorb liquids and liquid-containing waste released by the

attracted animal (see, *e.g.*, U.S. Patent No. 5,415,131).

Synthetic Perfumes. A "perfume" or a "fragrance composition" is a specific pleasantly odorous cosmetic composition for topical application to an individual. The olfactory receptor genes identified herein and those identified by the methods of the present invention may be used to identify chemicals which may be produced and used as synthetic perfumes. Such perfumes may be used to disguise odors or enhance attraction between humans (see, *e.g.*, U.S. Patent No. 5,278,141).

7. Pharmaceuticals. The olfactory receptor genes identified herein and those identified using the methods of the present invention may be used to identify pharmaceutical compounds useful for altering the behavior and physiology of animals. Examples of such compounds include, but are not limited to, certain Androstene steroids that effectuate a change in human hypothalamic function (see, *e.g.*, U.S. Patent No. 5,969,168).

8. Industrial Applications. The olfactory receptor genes identified by the methods of the present invention may be used for a number of different industrial applications including, but not limited to the following:

a) Identification of appetite suppressant compounds and using same to suppress and/or control appetite.

b) Trapping odors of a specific type.

c) As Biosensors.

1) Explosive and drug detectors. The detectors may be synthetic, such as biologically-inspired robotic sensors, or biological sensors, such as sniffing dogs which are especially sensitive to certain odors.

2) Population of olfactory receptor genes expressed in cell culture. Olfactory receptor genes can be introduced into a cell line and the transformed cells maintained in culture through multiple generations. By creating specific cell lines which express multiple olfactory genes at once, it would be possible to use such cell cultures to investigate how odorants interact with odorant receptor genes. Thus, the present invention provides methods for identifying odorant fingerprints, wherein such methods include contacting a series of cells

containing and expressing known odor receptor genes with a desired sample, and determining the type and quantity of the odorant ligands present in the sample (see, *e.g.*, U.S. Patent No. 5,993,778). As discussed elsewhere herein, the interaction of substances with the receptors can be identified using appropriate labels, such as those provided by luciferase, the jellyfish green fluorescent protein (GFP) or β -galactosidase.

3) Biochip Arrays. As discussed elsewhere herein, biochip arrays of odorant receptor genes can be generated. The arrays may be used to detect olfactory receptor ligands via an appropriate marker or via a chemical or electrical signal. Arrays may be designed for specific purposes, such as, but not limited to, detecting perfumes, explosives, drugs, pollutants, and toxins.

d) Training organisms to conduct certain tasks. Examples include, but are not limited to, the following:

1) Training mice to pull guide line for stringing fiber optic cable through existing conduit holding copper wire.

2) Training mice to find their way through a maze based on smell (see, *e.g.*, Otto *et al.*, (1991) *Hippocampus* 1, 181-192; Granger *et al.*, (1991) *Psych. Science* 2, 116-118).

3) Improving the orientation and homing performance of pigeons (see, *e.g.*, Wiltschko, (1996) *J. Exp. Biol.* 199, 113-119) and fish (see, *e.g.*, Cao *et al.* (1998) *Proc. Natl. Acad. Sci. USA* 95(20):11987-11992).

4) Orient or reorient the behavior of worker bees of a rearing colony by incorporating a composition which includes one or more pheromones which elicits particular bee behavior towards the larvae. Thus, the beekeeper may orient or reorient the bees towards a particular activity such as, but not limited to, inducing improved acceptance of the larvae at the beginning of rearing, to increase the production of royal jelly, regulate the feeding of the larvae as to favor the development of queen bees, etc. (see, *e.g.*, U.S. Patent No. 5,695,383).

Without further description, it is believed that one of ordinary skill in the art can, using the preceding description and the following illustrative examples, make and utilize the

compounds of the present invention and practice the claimed methods. The following working examples therefore, specifically point out the preferred embodiments of the present invention, and are not to be construed as limiting in any way the remainder of the disclosure.

5 **EXAMPLES**

Example 1: Identification of candidate olfactory receptor genes

In vertebrates and nematodes it is estimated that there are hundreds of olfactory receptor genes, widely distributed in the genome (Buck & Axel, (1991) Cell 65, 175-187; Troemel *et al.*, (1995) Cell 83, 207-218). With approximately 10% of the *Drosophila* genome sequenced, it was likely that some of the *Drosophila* odorant receptor genes have been sequenced. A two-step strategy was developed to identify odorant receptor genes from the genomic database. First, a computer algorithm was designed to search the *Drosophila* genomic sequence for open reading frames (ORFs) from candidate odorant receptor genes. Second, RT-PCR was used to determine if transcripts from any of these ORFs were expressed in olfactory organs. Finally, *in situ* hybridization was used to localize expression of DOR genes.

Step 1: Computer algorithm for identification of GPCR genes. The algorithm used to identify GPCR genes used statistical characterization of amino acid physico-chemical profiles in combination with a non-parametric discriminant function. The key approach is to use the information in the interplay between the local structure (transmembrane alpha helix) and the global structure (repeated multiple domains) and characterize this information with concise statistical variables. The algorithm was trained on a set of 100 putative GPCR sequences from the GPCR database (GPCRDB) at <http://swift.embl-heidelberg.de/7tm> and a set of 100 random proteins selected from the SWISSPROT database (this training set was later expanded, but that version was not used for the genes reported in this paper). In the first step, three sets of descriptors were used to summarize the physico-chemical profiles of the sequences. These were GES scale of hydropathy (Engelman *et al.*, (1986) Annu. Rev. Biophys. Biophys. Chem. 15, 321-353), polarity (Brown, (1991) Molecular Biology Labfax,

Academic Press), and amino acid usage frequency. For the first two of these measurements, a sliding window profile was employed (White, (1994) Membrane Protein Structure, Oxford University Press) using a kernel of 15 amino acid constant function convoluted with a 16 amino acid Gaussian function. These profiles were then summarized with three statistics; the periodicity (characterizing the quasi-periodic presence of the transmembrane domain), average derivative (characterizing the abrupt change between the transmembrane domain and non-transmembrane domain), and the variance of the derivative (also characterizing the abrupt change). GES periodicity, variance of polarity derivative, polarity periodicity and amino acid frequency were used as the four variables and each sequence was therefore characterized by four variables. These four variables were used in a non-parametric linear discriminant function that was then optimized to separate the known GPCRs from random proteins in the training set. The same linear discriminant function with the scores derived from the training set was then used to screen the genomic database for candidate genes. The candidate sequences were given significance values by an odds ratio of the GPCRs and non-GPCRs computed using the observed empirical distribution of the training set. More detailed information about the algorithm is available at <http://www.neuron.org/cgi/content/full/22/2/327/dc1>.

The computational screens used the genomic sequence data obtained by FTP from the Berkeley *Drosophila* Genome Project (BDGP, <http://www.fruitfly.org>, version 6/98). First, the ORFs of 300 bases or longer in all six frames were identified. Next, a program written to identify GPCRs statistically by their physico-chemical profile was used to screen for candidate ORFs as described above. The number of possible candidates was reduced by comparing them to *Drosophila* codon usage tables (<http://flybase.bio.indiana.edu>, version 10). Candidate ORFs whose codon usage differed at a significance level of 0.0005 by the chi-square statistic were discarded from the candidate set. Using these screening steps, 34 candidate ORFs were obtained.

Further analysis revealed that eight of the thirty-four candidate ORFs corresponded to genes of known function, for example a cyclic nucleotide-gated channel (Baumann *et al.*, (1994) EMBO J. 13, 5040-5050) and these ORFs were not further analyzed. Most of the

remaining ORFs encoded fewer than seven predicted transmembrane domains. The genomic DNA surrounding each of the computer-identified ORFs was therefore examined for the presence of neighboring ORFs encoding additional transmembrane domains to which the original ORFs might be spliced. *Drosophila* 5' and 3' intron-exon consensus splice sequences were used in this analysis to help identify linked exons (Mount *et al.*, (1992) Nucleic Acids Res. 20, 4255-4262). This analysis yielded several genes that encoded seven-transmembrane-domain proteins (22A.1 and 22A.2).

Step 2: Sequence analysis of DOR olfactory genes. To determine if these two candidates were part of a larger family of genes encoding seven-transmembrane-domain proteins, BLAST searches of the *Drosophila* genome database were conducted using the candidate gene sequences to identify related genes (Altschul *et al.*, (1990) J. Mol. Biol. 215, 403-410). The computer algorithms employed identified the ORFs for the second exons of 22A.1 and 22A.2, which encode transmembrane domains 1-4. These ORFs are on the BDGP P1 clone designated DS005342. The DS005342 sequence was examined around the initial ORFs for neighboring ORFs which encoded additional potential transmembrane domains. Key to the identification of these neighboring ORFs was the presence of intron-exon consensus splice sequences: GTRAGT for the 5' end and HAG for the 3' end (Mount *et al.*, (1992) Nucleic Acids Res. 20, 4255-4262). 22A.1 and 22A.2 were found to have two other introns in corresponding locations, all of which had conserved splice sequences.

The amino acid sequences of 22A.1 and 22A.2 were used in searches of the *Drosophila* genome database using the tBLASTn program of the BDGP. These searches yielded partial sequences of other members of the DOR family. To complete the sequences of these genes, an analysis of the genomic DNA around each identified ORF was carried out as was done for 22A.1 and 22A.2, using the locations of conserved introns in the genes, the intron consensus splice sequences, and the tBLASTn alignments as guides. Use of the genes identified in the second round as query sequences in tBLASTn searches and subsequent similar analysis of genomic DNA yielded the remaining genes. Additional searches of GenBank and SwissProt databases were performed with the NCBI (National Center for

Biotechnology Information) BLAST network.

The sequence alignment in Figure 3 is based on the alignments predicted by the tBLASTn program of the BDGP but was edited extensively. The 5' splice sequences for the most 3' introns of both 2F.1 and 47E.1 were unfavorable. It was assumed that these introns were spliced nonetheless, as the resulting amino acid sequence displayed greater sequence identity to other DOR family members. If these introns were not spliced out, then the lengths of 2F.1 and 47E.1 would not be significantly altered from the lengths indicated in Figure 3. 2F.1 was independently predicted to be a gene (GenBank accession number 2661571) by the EMBL genefinder program subsequent to the submission of the provisional application to which this application claims priority.

Homologs of the two candidates were found, and their sequences were used in turn for further database searches. In total, forty-nine genes have been identified from the approximately 16% genomic sequence currently available. Applicants have tentatively named this family of genes DOR (for *Drosophila* Olfactory Receptor), and each individual gene was named based upon its cytogenetic location in the genome. Thus the two genes identified initially are DOR22A.1 and DOR22A.2, which were abbreviated here as 22A.1 and 22A.2 (the final digit in this nomenclature is used to distinguish the genes at a site and does not refer to the cytogenetic band number). The genomic locations of all the DOR genes identified so far are indicated in Figure 2A, and an alignment of their amino acid sequences is presented in Figure 3. Of the forty-nine family members, the great majority have been found to be expressed in either the antenna or the maxillary palp, or in both, based upon RT-PCR analysis (Table 1) and *in situ* hybridizations to RNA in tissue sections.

The DOR genes have no significant similarities to any known genes, and do not appear in any of the *Drosophila* EST databases. However, Kyte-Doolittle hydropathy plots of the predicted proteins show that each has approximately seven peaks that could represent transmembrane domains (Figure 2C) (Kyte & Doolittle, (1982) J. Mol. Biol. 157, 105-132). The lengths of the sixteen proteins are between 369 and 403 amino acids, similar to the lengths of most previously described families of GPCRs (Probst *et al.*, (1992) DNA Cell Biol.

11, 1-20). In addition, the spacing of the putative transmembrane domains gives rise to predicted intracellular and extracellular loops similar in size to those in many families of GPCRs (Probst *et al.*, (1992) DNA Cell Biol. 11, 1-20).

Amino acid sequence identity among the DOR genes ranges from approximately 10-75%, with many genes showing a relatively low level of identity to each other (approximately 20%). Two pairs of clustered genes, 22A.1/22A.2 and 33B.1/33B.2 show the highest identity, with 75% and 57% homology, respectively. However, not all clustered genes show high degrees of similarity. 33B.3, for example, is only 28% identical to both 33B.1 and 33B.2 and 46F.1 and 46F.2 are only 29% identical. In addition to exhibiting sequence identity, many of the genes contain introns in corresponding locations (Figure 3), consistent with their constituting a family derived from a common ancestral gene. Examples of genomic DNA encoding the complete structural gene for DOR proteins containing the introns can be found in SEQ ID NO: 99-114, while the corresponding cDNA containing the intact ORF can be found in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29 and 31.

There are sixty-seven residues that are conserved among at least 50% of the genes, and most of these (49) are in the C-terminal halves of the proteins (Figure 3). Among the conserved residues are a serine and a threonine in the intracellular C-terminal tail, residues frequently conserved in this region of GPCRs (Probst *et al.*, (1992) DNA Cell Biol. 11, 1-20). The most divergent region in the sequences is a stretch of thirty amino acids representing part of the first extracellular loop and nearly all of transmembrane domain three. The divergence in this region also occurs in the most conserved pairs of genes: 22A.1 and 22A.2 are 75% identical overall, but only 50% identical in this region, and 33B.1 and 33B.2 are 57% identical overall, but only 33% identical in this region. This divergence has also been observed in other species. In particular, transmembrane domains three, four and five were exceptionally divergent in rat odorant receptors and have been proposed to play a role in odorant binding (Buck & Axel, (1991) Cell 65, 175-187).

Some of the genes are clustered in the genome (Figure 2A), while others are apparently isolated. Within a cluster the average intergenic distance is on the order of 500

bases. Clustered DOR genes do not necessarily have introns in corresponding locations (e.g. 46F.1 and 46F.2), but all clustered genes have their transcriptional orientations in the same direction (Figure 2A). At least one of the DOR genes (2F.1) is flanked closely on both sides by two apparently unrelated genes (Figure 2B) (Haenlin *et al.*, (1987) EMBO J. 6, 801-807).

5 A novel strategy to search the *Drosophila* genomic sequence database for genes encoding potential GPCRs was employed, leading to the identification of a multigene family with properties expected of odorant receptors. In addition to these genes, a wide variety of other transmembrane proteins were identified by this strategy, a few previously identified by other means and many representing novel proteins with similarity to known transmembrane
10 proteins. These results suggest that the algorithm may be of widespread use in identifying new receptors, channels, and other transmembrane proteins.

The family of candidate odorant receptor genes currently contains forty-nine members, identified from the 16% of the *Drosophila* genomic sequence that is available. By extrapolation the size of this family may be on the order of 100 genes, making it the largest
15 gene family identified in *Drosophila*.

There are several lines of evidence indicating that these genes encode *Drosophila* odorant receptors. First, the predicted proteins encoded by the genes each contain approximately seven potential transmembrane domains, as expected of GPCRs. Second, genes are expressed in one or both of the two olfactory organs, and for a number of genes this
20 expression is restricted to a subset of olfactory receptors, as expected for odorant receptors. Third, the large number of family members, and the clustered location of many of these genes in the *Drosophila* genome, is reminiscent of odorant receptors in other organisms.

Additional lines of evidence is available which indicates DOR proteins as odor receptors. First, antibodies raised against the product of the DOR22A.2 gene label a small
25 number of sensilla on the fly's antenna whose location corresponds to the same region labeled by *in situ* hybridization. Most important, staining appears localized to the cavities of the labeled sensilla, where the dendritic cells are located. This is exactly the localization expected of an odorant receptor. Second, different DOR genes are expressed (as determined by *in situ*

hybridization) in different subsets of olfactory receptor neurons, as expected of odor receptor genes. Third, as expected, the number of olfactory receptor neurons labeled by individual DOR genes corresponds with the number of olfactory receptor neurons exhibiting a particular odor-sensitivity because the number of neurons expressing a particular DOR gene is predicted to equal the number of neurons with a particular odor response spectrum. Finally, many of the DOR genes are not expressed in the Acj6 POU-domain transcription factor mutant, where a subset of olfactory receptor neurons displayed abnormal odorant specificities. A correlation between DOR gene expression and odorant-specificity therefore exists, as is expected with odorant receptor genes.

Comparison of the sequences of these candidate odorant receptors to those from other organisms shows that they are extremely divergent from known odorant receptors and other GPCR families. This is not surprising, as searches for these genes based on sequence similarity to odorant receptors from other organisms had not succeeded, and the odorant receptor families in vertebrates and *C. elegans* are essentially unrelated. There is a great deal of sequence divergence among the DOR genes, much more than among the rat sequences previously reported (Buck & Axel, (1991) Cell 65, 175-187), for example. Moreover, genomic Southern blots have shown that none of nine DOR genes tested defines a subfamily of more than two or so well-conserved genes. The DOR family therefore differs in this respect from the mouse family, for example, where most odorant receptor genes belong to subfamilies of approximately seven to ten genes (Ressler *et al.*, (1993) Cell 73, 597-609).

Although at present the clusters of DOR genes identified thus far contain smaller numbers of genes (less than three) than in other organisms (Troemel *et al.*, (1995) Cell 83, 207-218; Sullivan *et al.*, (1996) Proc. Natl. Acad. Sci. USA 93, 884-888; Barth *et al.*, (1997) Neuron 19, 359-369), a number of interesting features of the clustered genes are already apparent. As found in other organisms (Barth *et al.*, (1997) Neuron 19, 359-369), *Drosophila* odorant receptor genes within a cluster are not necessarily coordinately regulated, such that genes within a cluster are expressed in different classes of cells, and even in different olfactory organs (*e.g.* 46F.1 is expressed in the maxillary palp whereas 46F.2 is expressed in the

antenna). So far, all genes identified within a cluster, however, are transcribed in the same orientation. Genes within a cluster sometimes do, but sometimes do not, share intron positions, suggesting that introns may have become lost following gene duplication; a phylogenetic study revealed extensive gene duplication and intron loss among the chemoreceptor genes of *C. elegans* (Robertson, (1998) Genome Res. 8, 449-463).

Step 3: Identification of olfactory receptor genes using RT-PCR. RT-PCR with primers designed from two of these final candidates yielded amplification products from antennal cDNA. From RT-PCR experiments, the two genes did not appear to be expressed in the maxillary palp, abdomen, thorax, or head from which olfactory organs had been removed, suggesting that these genes were expressed specifically in the antenna. These two genes are located within 500 base pairs of each other at cytological position 22A (Figure 2A), and their predicted proteins are 75% homologous at the amino acid level.

For preparation of RNA, individual flies were frozen in liquid nitrogen, and antennae and maxillary palps were dissected. On average 150 antennae or 200 maxillary palps were used for RNA preparation. Total RNA was prepared as described elsewhere (McKenna *et al.*, (1994) J. Biol. Chem. 269, 16340-16347). The RNA was treated with DNaseI (Gibco-BRL) for thirty minutes at 37°C, phenol/chloroform extracted, and precipitated. The entire RNA preparation was used for oligo dT-primed cDNA synthesis using Superscript II Reverse Transcriptase (Gibco-BRL) according to the manufacturer's directions. PCR was performed using Taq polymerase (Sigma) under standard cycling conditions, with an annealing temperature of 60°C, gene-specific primer concentration of 1 pM, and magnesium concentration of 2.5 mM. For all genes except 2F.1, primer pairs which span introns were used in order to distinguish PCR bands amplified from cDNA from those amplified from any remaining genomic DNA.

Example 2: Hybridization of DOR gene probes to related sequences

To determine whether any of the DOR genes have closely related homologs, coding regions from nine of the genes were used to probe Southern blots of *Drosophila* genomic

DNA at high or low stringency. For the closely related genes such as 22A.1 and 22A.2, a combined probe was used. For genomic southern blots, hybridizations were at 65°C (high stringency) or 55°C (low stringency), in 7% SDS, 0.5 M sodium-phosphate buffer pH 7.2, 1 mM EDTA, pH 8.0.

5 Each probe detected only its own sequence at high stringency, while at low stringency most gene probes detected one or two novel bands (data not shown). As expected, because of the overall low level of similarity, none of these extra bands corresponded to any of the other known DOR genes. These data indicate that some of these genes have one or two closely related homologs, but that none belongs to a large subfamily of highly related genes.

10 Example 3: Localization of DOR gene expression

Olfactory receptor neurons of the adult fly are located in both the antenna and the maxillary palp. To ask whether any of the DOR genes are expressed in these neurons, *in situ* hybridization was carried out using adult tissue sections.

15 For *in situ* hybridization experiments, coding regions of the DOR genes were subcloned into the pGEM-T Easy vector (Promega). Digoxigenin-labeled RNA probes were generated and hydrolyzed according to the manufacturer's instructions (Boehringer Mannheim). *In situ* hybridizations to RNA in tissue sections were performed using a modified version of procedures described elsewhere (Roberts, (1998) *Drosophila: A Practical*
20 Approach, Oxford University Press; Chadwick & McGinnis, (1987) EMBO J. 6, 779-789). Briefly, heads were dissected from animals and fixed in 4% paraformaldehyde/PBS for fifteen minutes. Tween-20 was then added to 0.1% and heads were fixed for an additional thirty minutes. Samples were washed twice for five minutes in 0.1% Tween 20/PBS (PBST), cut into 8 µm frozen sections, and mounted on poly-L-Lysine treated slides (Sigma). Sections
25 were dried onto slides for thirty minutes at room temperature and then fixed for an additional thirty minutes in 4% paraformaldehyde/PBST. Samples were washed for a total of two hours in PBST with five changes of buffer, followed by an incubation for five minutes in 1:1 PBST:hybridization buffer (50% formamide, 5× SSC, 50 mg/ml heparin, 0.1% Tween 20),

and then prehybridized for two hours at 55°C.

Of eleven genes examined, seven displayed detectable expression, which in every case was restricted to the olfactory organs (Table 2). The 46F.1 probe hybridized to a subset of olfactory receptors in the maxillary palp (Figure 4A). Counting of labeled olfactory receptors in serial sections revealed that the total number of 46F.1-staining olfactory receptors per maxillary palp was 18 ± 1 (Table 2), or 15% of the 120 olfactory neurons in the maxillary palp. A similar number of neurons, 17 ± 1 , was labeled by another probe, 33B.3 (Figure 4B). The neuronal identity of the labeled cells was apparent from the presence in many cases of a well-defined axon projecting from the labeled cell body and joining the maxillary nerve (Figures 4B-C). For both probes, the labeled neurons were distributed broadly over the olfactory surface of the organ, and were interspersed among unlabeled neurons (Figures 4A-C). Staining in many cells appeared annular, which was interpreted to reflect a perinuclear distribution of mRNA, as expected of an mRNA present at highest concentrations in the cell bodies of these olfactory receptors (Figure 4B). The 33B.3 and 46F.1 genes are evidently expressed in different subsets of olfactory receptors, because the number of neurons hybridizing with a mixed probe was greater than the number of neurons that hybridized when either probe was used individually (data not shown). No hybridization detected in the antenna, head, or thorax for either probe.

Many of the DOR genes are expressed in the antenna and not in the maxillary palp, as determined by RT-PCR (Table 1). For several genes this localization was confirmed by *in situ* hybridization. The 47E.1 probe hybridized to 40 ± 1 cells in a broad area across the antenna (Figures 5A-B), including both anterior and posterior faces, similar to the distribution pattern of small *s. basiconica* (Figure 1F). A probe from the 25A.1 gene hybridized to fewer cells, 16 ± 1 , but in a region of the antenna similar to that of 47E.1 staining, as judged by reconstruction of serial sections (Figure 5C-D). The 22A.2 probe hybridized to 22 ± 1 cells in a different distribution, clustered in the dorso-medial region of the antenna (Figure 5E). This pattern matches the distribution of the large *s. basiconica* (Figure 1E). The expression patterns of the three genes in the antenna are illustrated schematically in Figure 5G. None of

these three probes revealed expression in the maxillary palp, head, or thorax. This data demonstrates that the DOR family is expressed in olfactory receptors, and that the expression of individual members is restricted to distinct subsets of cells in the olfactory organs.

The number and broad distribution of maxillary palp neurons expressing 46F.1 and 33B.3 are intriguing in light of electrophysiological studies. There are approximately 120 olfactory receptors on the palp, which fall into six different classes based upon their odorant response profiles. Each class contains roughly equal numbers of neurons, distributed broadly over the olfactory surface of the palp. Thus, if an individual receptor gene is expressed in all olfactory receptors of a functional class, one might expect a gene to be expressed in a broad distribution, in approximately twenty neurons, in good agreement with the distribution and numbers observed for both 46F.1 and 33B.3 (18 ± 1 and 17 ± 1 , respectively).

The two DOR genes whose expression was detected by *in situ* hybridization in the maxillary palp are expressed in olfactory receptors housed within s. basiconica, the only morphological class of sensilla on the palp. In the antenna, the 22A.2 probe consistently hybridized to a subset of cells in a portion of the dorso-medial region of the antenna that contains almost exclusively large s. basiconica (Figure 1E). The 47E.1 and 25A.1 probes hybridize to subsets of cells in a distinctly different region of the antenna which may correlate with the distribution of small s. basiconica, of which at least two functional types are intermingled (Figure 1F). Of particular interest, the numbers of cells to which 47E.1 and 25A.1 hybridize are different: 40 ± 1 and 16 ± 1 ; one possible interpretation is that they are expressed in distinct functional types of small s. basiconica. This region also contains s. trichodea and s. coeloconica, and although the labeling patterns do not correlate with the distribution of either of two functional classes of s. trichodea (Clyne *et al.*, (1997) Invert. Neurosci. 3, 127-135), a definitive identification of the sensillar type may require further investigation. If in fact all the DOR genes are expressed in only one of the morphological categories of sensilla, the s. basiconica, it is possible that there are other, as yet unidentified, families of receptors that are expressed in the other morphological categories of sensilla. This would mean that the number of odorant receptors in *Drosophila* might be substantially larger

than one-hundred.

Applicants have identified three DOR genes that are expressed in the maxillary palp (Table 1), from the 16% of the genome analyzed. As these three genes, like most DOR genes, are not clustered in the genome, linear extrapolation suggests that the entire genome contains on the order of eighteen DOR genes expressed in the maxillary palp, an organ which has six functional classes of neurons (Clyne *et al.*, (1999) Neuron 22, 339-347; de Bruyne *et al.*, (1999) J. Neurosci. 19, 4520-4532). If all neurons within a functional class, *i.e.* with the same odor-specificity, are identical in terms of their receptor expression, then the ratio of expressed genes to neuronal classes in this organ would be consistent with a model in which an individual ORN expresses a small number of odorant receptors; however, further data is needed to establish conclusively the number of receptor genes expressed per cell. Olfactory neurons in other organisms appear to lie at either of two extremes: in the vertebrates, it is believed only one receptor is expressed per ORN (Ngai *et al.*, (1993) Cell 72, 667-680; Ressler *et al.*, (1993) Cell 73, 597-609; Vassar *et al.*, (1993) Cell 74, 309-318); in *C. elegans*, approximately 550 chemoreceptors are likely to be distributed amongst fourteen classes of chemosensory neurons (Troemel *et al.*, (1995) Cell 83, 207-218).

Olfactory receptors in *Drosophila* and other insects project to an olfactory processing center, the antennal lobe, which is much like the olfactory bulb of vertebrates. Like its vertebrate counterpart, the antennal lobe contains olfactory glomeruli, of which the antennal lobe of *Drosophila* has approximately forty (Stocker *et al.*, (1995) Roux's Arch Dev Biol 205, 62-72; Laissue *et al.*, (1999) J. Comp. Neurol. 405, 543-552). In vertebrates there is an approximate equivalence between the estimated number of odorant receptor genes and the number of glomeruli (Barth *et al.*, (1996) Neuron 16, 23-34; Buck, (1996) Annu. Rev. Neurosci. 19, 517-544); since *C. elegans* does not contain glomeruli, it has not been possible until now to consider whether the evolutionary conservation of this equivalence extends to invertebrates. If in fact the number of DOR genes is one-hundred, then the ratio of odorant receptor genes to glomeruli would exceed two, and would rise if additional families of odorant receptor genes were discovered. Of particular interest, the number of glomeruli receiving

input from the maxillary palp has been variously estimated as three and five (Venkatesh & Singh, (1984) Int. J. Insect. Morphol. Embryol. 13, 51-63; Stocker *et al.*, (1995) Roux's Arch Dev Biol 205, 62-72); if our estimate of eighteen genes expressed in the maxillary palp is correct, then the ratio of these receptor genes to their corresponding glomeruli would fall in the range of three to six.

Example 4: DOR gene expression during development

Recent evidence supports a dual role for the vertebrate olfactory receptors. First, these receptors have an instructive role in guiding the axons of olfactory receptors to the correct glomeruli during development (Mombaerts *et al.*, (1996) Cell 87, 675-686; Wang *et al.*, (1998) Cell 93, 47-60), and second as odorant receptors in the adult (Zhao *et al.*, (1998) Science 279, 237-242). To address the possibility that the DOR genes might also play a role in development, three DOR probes were hybridized to antennal sections from different stages of pupal development. In *Drosophila*, ORN axons first leave the developing antenna at approximately sixteen hours after puparium formation (APF) (Lienhard & Stocker, (1991) Development 112, 1063-1075; Ray & Rodrigues, (1995) Dev. Biol. 167, 426-438; Reddy *et al.*, (1997) Development 124, 703-712), and the diameter of the antennal nerve continues to increase until 72 hours APF (Stocker *et al.*, (1995) Roux's Arch. Dev. Biol. 205, 62-72). Glomeruli first become visible in the antennal lobe at approximately 48 hours APF. Developing antennae were therefore examined at 16, 24, 36, 48, 54, 60, 72 and 93 hours APF (adults eclosed from the pupal case at approximately 100 hours). For these developmental studies, *Drosophila* were collected as white prepupae and kept at 25°C on moist filter paper for the indicated number of hours, at which time they were fixed. At 25°C the approximate time from the white prepupal stage to eclosion is 100 hours (Lockett & Ashburner, (1989) Dev. Biol. 134, 430-437).

Cells positive for 22A.2 were first seen at 60 hours APF, indicating that detectable expression begins between 54 and 60 hours, well within the period in which the antennal nerve is still increasing in diameter (Figure 6A-B). A subset of cells was labeled at this time,

and they were restricted to a subregion of the developing antenna; the pattern appears comparable to that of the mature antenna, although this pattern was not characterized in as much detail as that of the adult. Labeling with 22A.2 was also observed in antennae at all subsequent time points. Interestingly, cells positive for 47E.1 and 25A.1 were not observed until much later, at the 93 hour time point; they were not observed at any of the earlier times (Figure 6C-D and data not shown). For comparison, *in situ* hybridization was also performed with a probe representing the odorant-binding protein OS-E (McKenna *et al.*, (1994) J. Biol. Chem. 269, 16340-16347), which is believed to play a role in olfactory function, but which has not been implicated in a developmental process. OS-E was also first observed at 93 hours, at which time its expression increased (Figure 6E-F).

Example 5: Regulation of DOR expression by POU domain transcription factor *acj6*

Little is known about the regulation of odor receptor genes, a process critical to the establishment of olfactory neuron identity and ultimately to the process of olfactory coding. In *C. elegans* the *odr7* gene, a member of the nuclear receptor superfamily, has been shown to regulate the odorant receptor gene *odr10* (Sengupta *et al.*, (1994) Cell 79, 971-980; Sengupta *et al.*, (1996) Cell 84, 899-909). In *Drosophila*, null mutations of the *acj6* gene, which encodes a POU domain transcription factor, eliminate the odor response of three of the six classes of maxillary palp olfactory receptors (Clyne *et al.*, (1999) Neuron 22, 339-347). A fourth ORN class on the maxillary palp is altered to a new class of ORN with a novel odor sensitivity. These data suggest that Acj6 plays a role in the differentiation of certain maxillary palp olfactory receptors, perhaps by determining which olfactory receptor gene(s) are expressed. To address the possibility that Acj6 regulates odorant receptor genes, probes from the 33B.3 and 46F.1 genes were hybridized to sections of maxillary palps from the null mutant, *acj6*⁰. No hybridization was detected in either case (Figure 4D and data not shown), nor was expression of either gene detected by RT-PCR from *acj6*⁰ maxillary palps (Table 1).

acj6 mutations also affect the physiological response of the antennal neurons to odors (Ayer & Carlson, (1991) Proc. Nat. Acad. Sci. USA 88, 5467-5471; Ayer & Carlson, (1992)

J. Neurobiol. 23, 965-982). 22A.2, 25A.1, and 47E.1 probes were therefore hybridized to sections of *acj6*⁶ antennae. All three probes hybridized to groups of cells in the same locations as in the wild type antenna (Figure 5F and data not shown). RT-PCR amplification showed that expression of certain other DOR genes, 33B.1, 33B.2, 33B.3, and 46F.2 was eliminated in the antenna of *acj6*⁶ (Table 1). Thus, in the *acj6*⁶ mutant, one subset of candidate odorant receptor genes was not expressed while a different subset remained unaffected. Interestingly, genes within a cluster all showed similar dependency on Acj6: 33B.1, 33B.2, and 33B.3, for example, all depended on Acj6, whereas 22A.1 and 22A.2 did not. In summary, these data support a role for *acj6* in the regulation of a subset of olfactory receptor genes.

The DOR family is subject to complex regulation. First, the expression of individual DOR genes exhibits highly specific tissue and spatial localization. Some genes are expressed in the antenna but not the maxillary palp; others show expression in the maxillary palp but not the antenna. Within an organ, expression of a particular DOR gene is restricted to a subset of cells. In the antenna, the patterns of expression are spatially regulated, exhibiting regional specificity of expression as detailed above. In the maxillary palp, expression is limited to a population of neurons approximately equal in number to the neurons of a functional class.

DOR genes are also subject to interesting temporal regulation. One gene, 22A.2, is expressed in the developing antenna during a time when the antennal nerve is still increasing in diameter (Stocker *et al.*, (1995) Roux's Arch. Dev. Biol. 205, 62-72). These data leave open a possible role for *Drosophila* olfactory receptors in axon guidance and glomerulus formation, a role for which evidence has been found in vertebrates (Mombaerts *et al.*, (1996) Cell 87, 675-686; Wang *et al.*, (1998) Cell 93, 47-60) but not *C. elegans*. In zebrafish, odorant receptors show asynchronous onset of expression during development of the olfactory placode (Barth *et al.*, (1996) Neuron 16, 23-34). The DOR genes also show heterogeneity in their temporal regulation: expression of two other DOR genes begins much later than for the 22A.2 gene. If in fact individual olfactory receptors express more than one DOR gene, perhaps some have acquired a specialized role in development.

Evidence also exists indicating that different DOR genes are expressed at different

levels of abundance within cells. Although RT-PCR experiments demonstrated expression of 25A.1 in both antenna and maxillary palp, *in situ* hybridization revealed expression of 25A.1 only in the antenna of each animal examined; conversely, although RT-PCR experiments showed expression of 33B.3 in both olfactory organs, *in situ* hybridization detected label only in the maxillary palp of each animal examined (Tables 1 and 2). These results suggest that a receptor gene may be expressed at different cellular levels in the two organs, and that different genes may be expressed at different cellular levels in the same organ. Such an explanation would suggest that there are mechanisms governing not only the spatial and temporal control of DOR genes, but also their levels of expression.

If DOR genes are in fact expressed at different cellular levels in particular olfactory receptors, then perhaps the four DOR genes that were undetectable in the antenna by *in situ* hybridization, despite clear evidence for their antennal expression from RT-PCR, a more sensitive technique, are among those expressed at low levels. It is important to note that in *C. elegans*, expression of a number of candidate odorant receptors was undetectable using GFP fusion genes (Troemel *et al.*, (1995) Cell 83, 207-218).

As a first step in investigating the mechanisms through which the complex regulation of DOR genes is achieved, the role of the POU domain transcription factor Acj6 was tested, which was previously found to act in governing olfactory neuron identity. Applicants found that Acj6 is in fact required for expression of the DOR family. Two lines of evidence, RT-PCR and *in situ* hybridization analysis, both indicate that proper expression of a specific subset of DOR genes depends on Acj6. The results indicate that the odor-specificity of a subset of olfactory receptors is governed at least in part by the action of the Acj6 POU domain transcription factor on DOR genes, and are fully consistent with the notion that DOR genes encode odorant receptors.

The isolation of genes likely to encode odorant receptors in *Drosophila* opens a number of avenues for future investigation. *Drosophila* provides the ability to manipulate odor receptors genetically and test the functional consequences of such manipulations *in vivo*, either physiologically or behaviorally. Such analysis may be useful in examining potential

roles of DOR proteins in olfactory response and in development. It may also be possible to isolate homologous genes in other insects, including some which provide excellent opportunities for research and some of agricultural or medical importance which rely on olfactory cues to locate their hosts.

5

Example 6: Transgenic *Drosophila*

P element mediated germline transformation of *Drosophila* can be carried out as previously described (Rubin & Spradling, (1982) Science 218, 348-353). *Drosophila* embryos are isolated and microinjected with P element expression constructs as previously described (Karess & Rubin, (1984) Cell 38, 135-146) containing a particular DOR nucleotide sequence, at 0.5 mg/ml together with a helper plasmid at 0.1 mg/ml. G₀ injected adults are individually back crossed to the recipient strain and the G₁ progeny screened for the w⁺ transformation marker (Klemenz *et al.*, (1987) Nucleic Acids Res. 10, 3947-3959).

10

Transformed lines homozygous for the transgene are established from orange eyed G₁ flies as previously described (Klemenz *et al.*, (1987) Nucleic Acids Res. 10, 3947-3959).

15

A line of *Drosophila* in which the DOR33B.3 gene can be over-expressed was constructed as described above. The DOR33B.3 coding sequences were joined to an upstream activating sequence (UAS) and introduced by P element-mediated germline transformation into *Drosophila*. A yeast GAL4 transcription factor gene, coupled to a heat shock promoter, was then crossed into the transgenic line. As expected, heat shock of this line resulted in induction of DOR33B.3 expression. The heat shock-induced expression of GAL4, results in binding of GAL4 to the UAS, and subsequent induction of DOR33B.3 expression. This transgenic line of *Drosophila*, and three other transgenic lines containing other DOR genes, can be tested for elevated responses to any of fifty different odors. Elevated response to any particular odorant is indicative of an ligand which binds and activates the over-expressed receptor (see, *e.g.*, Zhao & Firestein, (1998) Science 279, 237-242).

20

25

Although the present invention has been described in detail with reference to

examples above, it is understood that various modifications can be made without departing from the spirit of the invention. Accordingly, the invention is limited only by the following claims. All cited patents and publications referred to in this application are herein incorporated by reference in their entirety. The results of the experiments disclosed herein

5 have been published in the journal Neuron (22, 327-338) in February, 1999, this article herein incorporated by reference in its entirety.

We claim:

1. An isolated nucleic acid molecule selected from the group consisting of:

a) an isolated nucleic acid molecule that encodes the amino acid sequence of a

5 *Drosophila* Odorant Receptor protein;

b) an isolated nucleic acid molecule that encodes a protein fragment of at least 6 amino acids of a *Drosophila* Odorant Receptor protein; and

c) an isolated nucleic acid molecule which hybridizes to a nucleic acid molecule comprising a nucleotide sequence encoding a *Drosophila* Odorant Receptor protein under
10 conditions of sufficient stringency to produce a clear signal.

2. The isolated nucleic acid molecule of claim 1 wherein the nucleic acid comprises at least one exon-intron boundary located in a position selected from the group consisting of:

a) the nucleotides encoding the amino acids which comprise the third extracellular
15 domain of a *Drosophila* Odorant Receptor protein;

b) the nucleotides encoding the amino acids which comprise the fourth extracellular domain of a *Drosophila* Odorant Receptor protein; and

c) the nucleotides encoding the amino acids which comprise the fourth intracellular domain of a *Drosophila* Odorant Receptor protein.
20

3. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is selected from the group consisting of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95 and 97.
25

4. The isolated nucleic acid molecule of any one of claims 1-3, wherein said nucleic acid molecule is operably linked to one or more expression control elements.

5. A vector comprising an isolated nucleic acid molecule of any one of claims 1-3.

6. A host cell transformed to contain the nucleic acid molecule of any one of claims 1-3.

5

7. A host cell comprising a vector of claim 5.

8. A host cell of claim 7, wherein said host is selected from the group consisting of prokaryotic hosts and eukaryotic hosts.

10

9. A method for producing a protein or protein fragment comprising the step of culturing a host cell transformed with the nucleic acid molecule of any one of claims 1-3 under conditions in which the protein or protein fragment encoded by said nucleic acid molecule is expressed.

15

10. The method of claim 9, wherein said host cell is selected from the group consisting of prokaryotic hosts and eukaryotic hosts.

11. An isolated protein or protein fragment produced by the method of claim 10.

20

12. An isolated protein or protein fragment selected from the group consisting of:

a) an isolated protein comprising one of the amino acid sequences depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96 and 98;

25

b) an isolated protein fragment comprising at least 6 amino acids of any of the sequences depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96 and 98;

c) an isolated protein comprising conservative amino acid substitutions of any of the sequences depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96 and 98; and

5 d) naturally occurring amino acid sequence variants of any of the sequences depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96 and 98.

10 13. The isolated protein or protein fragment of claim 12 wherein the protein or protein fragment has at least one of the following conserved amino acids selected from the group consisting of:

a) Leucine in the third extracellular domain of a *Drosophila* Odorant Receptor protein;

15 b) Histidine in the third extracellular domain of a *Drosophila* Odorant Receptor protein;

c) Cysteine in the sixth transmembrane domain of a *Drosophila* Odorant Receptor protein;

d) Tryptophan in the fourth extracellular domain of a *Drosophila* Odorant Receptor protein;

20 e) Glutamine in the seventh transmembrane domain of a *Drosophila* Odorant Receptor protein;

f) Proline in the seventh transmembrane domain of a *Drosophila* Odorant Receptor protein;

25 g) Alanine in the fourth intracellular domain of a *Drosophila* Odorant Receptor protein; and

h) Tyrosine in the fourth intracellular domain of a *Drosophila* Odorant Receptor protein.

14. An isolated antibody that binds to a polypeptide of claim 11, 12 or 13.

15. The antibody of claim 14 wherein said antibody is a monoclonal or polyclonal antibody.

5

16. A method of identifying an agent which modulates the expression of a protein or protein fragment of claim 11, 12 or 13 comprising the steps of:

a) exposing cells which express the protein or protein fragment to the agent; and

b) determining whether the agent modulates expression of said protein or protein fragment, thereby identifying an agent which modulates the expression of a protein or protein fragment of claim 11, 12 or 13.

10

17. A method of identifying an agent which modulates the activity of a protein or protein fragment of claim 11, 12 or 13 comprising the steps of:

a) exposing cells which express the protein or protein fragment to the agent; and

15

b) determining whether the agent modulates the activity of said protein or protein fragment, thereby identifying an agent which modulates the activity of a protein or protein fragment of claim 11, 12 or 13.

20

18. The method of claim 17, wherein the agent modulates at least one activity of the protein or protein fragment.

19. A method of identifying an agent which modulates the transcription of the nucleic acid molecule of any one of claims 1-3 comprising the steps of:

25

a) exposing cells which transcribe the nucleic acid to the agent; and

b) determining whether the agent modulates transcription of said nucleic acid, thereby identifying an agent which modulates the transcription of the nucleic acid molecule of any one of claims 1-3.

20. A method of identifying binding partners for a protein or protein fragment of either claim 11, 12 or 13 comprising the steps of:

- a) exposing said protein or protein fragment to a potential binding partner; and
 - b) determining if the potential binding partner binds to said protein or protein
- 5 fragment, thereby identifying binding partners for the protein or protein fragment.

21. A method of modulating the expression of a nucleic acid encoding a protein or protein fragment of claim 11, 12 or 13 comprising administering an effective amount of an agent which modulates the expression of a nucleic acid encoding the protein or protein

10 fragment.

22. A method of modulating at least one activity of a protein or protein fragment of claim 11, 12 or 13 comprising the step of administering an effective amount of an agent which modulates at least one activity of the protein or protein fragment.

23. A method of identifying novel olfactory receptor genes comprising the steps of:

- a) selecting candidate olfactory receptor genes by screening a nucleic acid database using an algorithm trained to identify seven transmembrane receptors genes;

- b) screening said selected candidate olfactory receptor genes by identifying nucleic

20 acid sequences with conserved amino acid residues and intron-exon boundaries common to olfactory receptors, and having open reading frames of sufficient size so as to encode a seven transmembrane receptor; and

- c) identifying the novel olfactory receptor genes and measuring the expression of olfactory receptor genes wherein the detection of expression confirms said candidate olfactory

25 gene as an olfactory gene.

24. A method of identifying novel olfactory receptor genes comprising the steps of:

- a) selecting candidate olfactory receptor genes by screening a nucleic acid database for

nucleic acid sequences with sufficient homology to at least one known olfactory receptor gene;

b) screening said selected candidate olfactory receptor genes by identifying nucleic acids with conserved amino acid residues and intron-exon boundaries common to olfactory
5 receptors, and having open reading frames of sufficient size so as to encode a seven transmembrane receptor; and

c) identifying the novel olfactory receptor genes and measuring the expression of olfactory receptor genes wherein the detection of expression confirms said candidate olfactory gene as an olfactory gene.

10

25. A transgenic insect modified to contain a nucleic acid molecule of any of claims 1-3.

15

26. The transgenic insect of claim 25, wherein the nucleic acid molecule contains a mutation that alters expression of the encoded protein.

ABSTRACT

The present invention provides nucleic acids and amino acids for novel olfactory receptors as well as methods for identifying olfactory receptors. More specifically, the present invention provides nucleic acids and amino acids for novel olfactory receptors in

5 *Drosophila* as well as methods of using the provided nucleic acids and amino acids. In addition, this invention provides methods of identifying ligands which bind to the novel olfactory receptors as well as a variety of methods for using the ligands so identified.

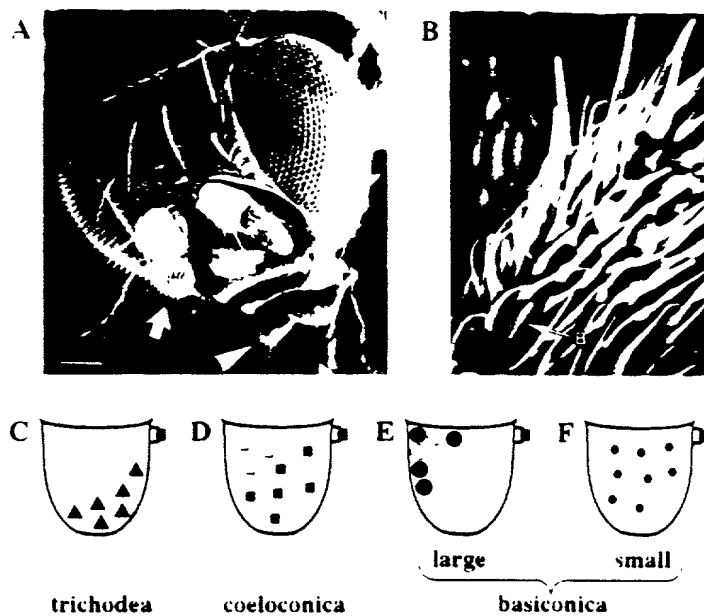


Figure 1

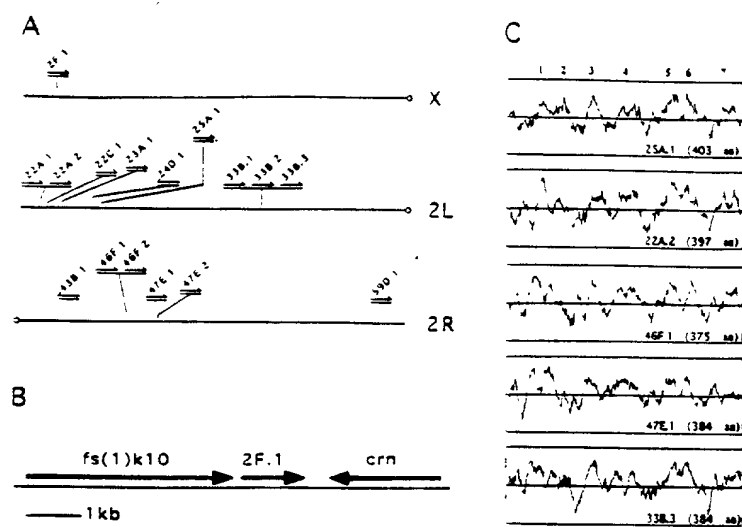


Figure 2

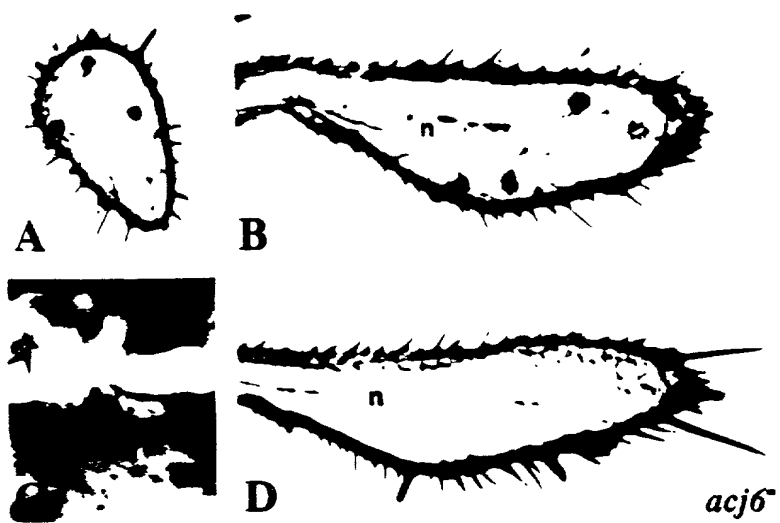


Figure 4

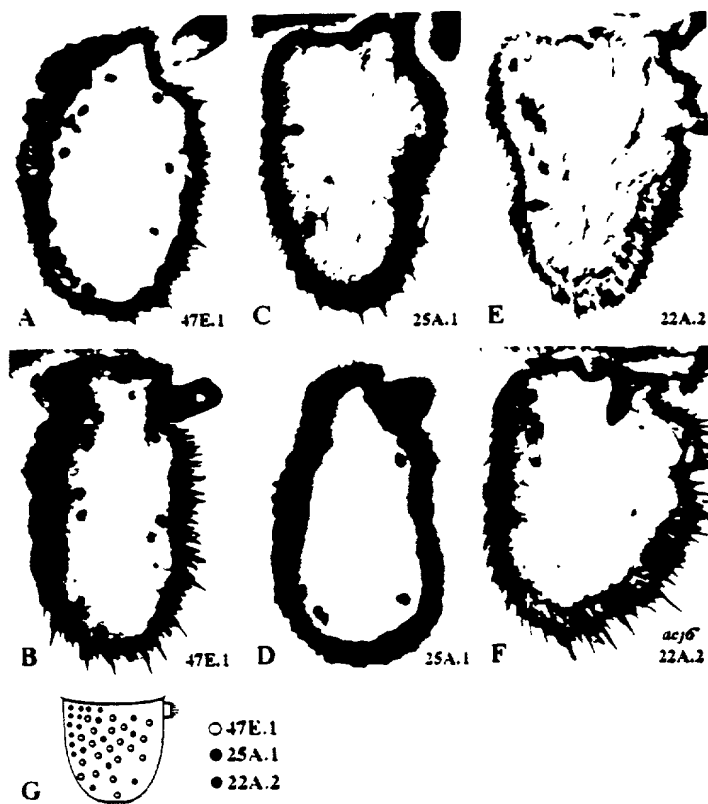


Figure 5



Figure 6

ic511 U.S. PTO
09/491577
01/25/00

John R. Carlson *et al.*

Group Art Unit:

Examiner:

For: NOVEL FAMILY OF ODORANT
RECEPTORS IN DROSOPHILA

Assistant Commissioner for Patents
Washington, D.C. 20231
BOX SEQUENCE

STATEMENT ACCOMPANYING SEQUENCE LISTING

Dear Sir:

The undersigned hereby states upon information and belief that the Sequence Listing submitted concurrently herewith does not include matter which goes beyond the content of the application as filed and that the information recorded on the diskette submitted concurrently herewith is identical to the written Sequence Listing submitted herewith.

Respectfully submitted,

MORGAN, LEWIS & BOCKIUS LLP

Dated: January 25, 2000

By: Rosanne Kosson
Printed Name: Rosanne Kosson

MORGAN, LEWIS & BOCKIUS LLP
1800 M Street, N.W.
Washington, D.C. 20036
(202) 467-7000
Express Mail No.: EI149177978US

SEQUENCE LISTING

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Carlson, John R.
Kim, Hunhyong
Clyne, Peter J.
Warr, Coral G.

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		35						40					45			

aaa	ctg	tgg	tca	act	ttc	gtg	aca	ttg	ttg	ata	ttt	atc	ctt	ctg	ccg	192
Lys	Leu	Trp	Ser	Thr	Phe	Val	Thr	Leu	Leu	Ile	Phe	Ile	Leu	Leu	Pro	
	50						55				60					

<210> 2
 <211> 255
 <212> PRT
 <213> Drosophila melanogaster

<400> 2

Met Leu Ser Gln Phe Phe Pro His Ile Lys Glu Lys Pro Leu Ser Glu
 1 5 10 15

Arg Val Lys Ser Arg Asp Ala Phe Val Tyr Leu Asp Arg Val Met Trp
 20 25 30

Ser Phe Gly Trp Thr Val Pro Glu Asn Lys Arg Trp Asp Leu His Tyr
 35 40 45

Lys Leu Trp Ser Thr Phe Val Thr Leu Leu Ile Phe Ile Leu Leu Pro
 50 55 60

Ile Ser Val Ser Val Glu Tyr Ile Gln Arg Phe Lys Thr Phe Ser Ala
 65 70 75 80

Gly Glu Phe Leu Ser Ser Ile Gln Ile Gly Val Asn Met Tyr Gly Ser
 85 90 95

Ser Phe Lys Ser Tyr Leu Thr Met Met Gly Tyr Lys Lys Arg Gln Glu
 100 105 110

Ala Lys Met Ser Leu Asp Glu Leu Asp Lys Arg Cys Val Cys Asp Glu
 115 120 125

Glu Arg Thr Ile Val His Arg His Val Ala Leu Gly Asn Phe Cys Tyr
 130 135 140

Ile Phe Tyr His Ile Ala Tyr Thr Ser Phe Leu Ile Ser Asn Phe Leu
 145 150 155 160

Ser Phe Ile Met Lys Arg Ile His Ala Trp Arg Met Tyr Phe Pro Tyr
 165 170 175

Val Asp Pro Glu Lys Gln Phe Tyr Ile Ser Ser Ile Ala Glu Val Ile
 180 185 190

Leu Arg Gly Trp Ala Val Phe Met Asp Leu Cys Thr Asp Val Cys Pro
 195 200 205

Leu Ile Ser Met Val Ile Ala Arg Cys His Ile Thr Leu Leu Lys Gln

220

Leu Lys Glu Leu Ala Asp Cys Val Arg Asp His Arg Leu Ile Leu
245 250 255

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<220>
<221> CDS
<222> (1)..(1137)
<223> DOR 22C.1, a coding segment on BDGP Clone No.
AC004716
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<400> 3																	
atg	act	gac	agc	ggg	cag	cct	gcc	att	gcc	gac	cac	ttt	tat	cgg	att	48	
Met	Thr	Asp	Ser	Gly	Gln	Pro	Ala	Ile	Ala	Asp	His	Phe	Tyr	Arg	Ile		
1				5				10				15					
ccc	cgc	atc	tcc	ggc	ctc	att	gtc	ggc	ctc	tgg	ccg	caa	agg	ata	agg	96	
Pro	Arg	Ile	Ser	Gly	Leu	Ile	Val	Gly	Leu	Trp	Pro	Gln	Arg	Ile	Arg		
20				25				30									
ggc	ggg	ggc	ggt	cgt	cct	tgg	cac	gcc	cat	ctg	ctc	ttc	gtg	ttc	gcc	144	
Gly	Gly	Gly	Gly	Arg	Pro	Trp	His	Ala	His	Leu	Leu	Phe	Val	Phe	Ala		
35				40				45									
ttc	gcc	atg	gtg	gtg	gtg	ggt	gcg	gtg	ggc	gag	gtg	tcg	tac	ggc	tgt	192	
Phe	Ala	Met	Val	Val	Val	Gly	Ala	Val	Gly	Glu	Val	Ser	Tyr	Gly	Cys		
50				55				60									
gtc	cac	ctg	gac	aac	ctg	gtg	gtg	gcg	ctg	gag	gcc	ttc	tgc	ccc	gga	240	
Val	His	Leu	Asp	Asn	Leu	Val	Val	Ala	Leu	Glu	Ala	Phe	Cys	Pro	Gly		
65				70				75				80					
acc	acc	aag	gcg	gtc	tgc	gtt	ttg	aag	ctg	tgg	gtc	ttc	ttc	cgc	tcc	288	
Thr	Thr	Lys	Ala	Val	Cys	Val	Leu	Lys	Leu	Trp	Val	Phe	Phe	Arg	Ser		
85				90				95									
aat	cgc	cgg	tgg	gcg	gag	ttg	gtc	cag	cgc	ctg	cgg	gct	att	ttg	ctc	336	
Asn	Arg	Arg	Trp	Ala	Glu	Leu	Val	Gln	Arg	Leu	Arg	Ala	Ile	Leu	Leu		

300

ggc tca tat atc acg ctg cta aag acg ttc ctg taa 1140
Gly Ser Tyr Ile Thr Leu Leu Lys Thr Phe Leu
370 375

<213> Drosophila melanogaster

Asn Arg Arg Trp Ala Glu Leu Val Gln Arg Leu Arg Ala Ile Leu Leu

100	105	110
Ser Leu Leu Leu Leu Ser Ser Gly Thr Ala Thr Asn Ala Ala Phe Thr		
115	120	125
Leu Gln Pro Leu Ile Met Gly Leu Tyr Arg Trp Ile Val Gln Leu Pro		
130	135	140
Gly Gln Thr Glu Leu Pro Phe Asn Ile Ile Leu Pro Ser Phe Ala Val		
145	150	155
Gln Pro Gly Val Phe Pro Leu Thr Tyr Val Leu Leu Thr Ala Ser Gly		
165	170	175
Ala Cys Thr Val Phe Ala Phe Ser Phe Val Asp Gly Phe Phe Ile Cys		
180	185	190
Ser Cys Leu Tyr Ile Cys Gly Ala Phe Arg Leu Val Gln Gln Asp Ile		
195	200	205
Arg Arg Ile Phe Ala Asp Leu His Gly Val Asp Val Phe Thr Glu Glu		
210	215	220
Met Asn Ala Glu Val Arg His Arg Leu Ala Gln Val Val Glu Arg His		
225	230	235
Asn Ala Ile Ile Asp Phe Cys Thr Asp Leu Thr Arg Gln Phe Thr Val		
245	250	255
Ile Val Leu Met His Phe Leu Ser Ala Ala Phe Val Leu Cys Ser Thr		
260	265	270
Ile Leu Asp Ile Met Leu Asn Thr Ser Ser Leu Ser Gly Leu Thr Tyr		
275	280	285
Ile Cys Tyr Ile Ile Ala Ala Leu Thr Gln Leu Phe Leu Tyr Cys Phe		
290	295	300
Gly Gly Asn His Val Ser Glu Ser Ser Ala Ala Val Ala Asp Val Leu		
305	310	315
Tyr Asp Met Glu Trp Tyr Lys Cys Asp Ala Arg Thr Arg Lys Val Ile		
325	330	335
Leu Met Ile Leu Arg Arg Ser Gln Arg Ala Lys Thr Ile Ala Val Pro		
340	345	350
Phe Phe Thr Pro Ser Leu Pro Ala Leu Arg Ser Ile Leu Ser Thr Ala		

355

360

365

Gly Ser Tyr Ile Thr Leu Leu Lys Thr Phe Leu
370 375

<210> 5

<211> 1140

<212> DNA

<213> Drosophila melanogaster

<220>

<221> CDS

<222> (1) .. (1137)

<223> DOR23A.1, coding region of AF127925

<400> 5

atg aag ctc agc gaa acc cta aaa atc gac tat ttt cga gtc cag ttg 48
Met Lys Leu Ser Glu Thr Leu Lys Ile Asp Tyr Phe Arg Val Gln Leu
1 5 10 15

aat gcc tgg cga att tgt ggt gcc ttg gat ctc agc gag ggt agg tac 96
Asn Ala Trp Arg Ile Cys Gly Ala Leu Asp Leu Ser Glu Gly Arg Tyr
20 25 30

tgg agt tgg tcg atg cta ttg tgc atc ttg gtg tac ctg ccg aca ccc 144
 Trp Ser Trp Ser Met Leu Leu Cys Ile Leu Val Tyr Leu Pro Thr Pro
 35 40 45

atg cta ctg aga gga gta tac agt ttc gaa gat ccg gtg gaa aat aat 192
Met Leu Leu Arg Gly Val Tyr Ser Phe Glu Asp Pro Val Glu Asn Asn
50 55 60

ttc agc ttg agc ctg acg gtc act tcg ctg tcc aat ctc atg aag ttc 240
Phe Ser Leu Ser Leu Thr Val Thr Ser Leu Ser Asn Leu Met Lys Phe
65 70 75 80

tgc atg tac gtg gcc caa cta aca aag atg gtc gag gtc cag agt ctt 288
Cys Met Tyr Val Ala Gln Leu Thr Lys Met Val Glu Val Gln Ser Leu
85 90 95

att ggt cag ctg gat gcc cgg gtt tct ggc gag agc cag tct gag cgt 336
Ile Gly Gln Leu Asp Ala Arg Val Ser Gly Glu Ser Gln Ser Glu Arg
100 105 110

cat aga aat atg acc gag cac ctg cta agg atg tcc aag ctg ttc cag 384
His Arg Asn Met Thr Glu His Leu Leu Arg Met Ser Lys Leu Phe Gln

125

cag gag agt ttt gct gag ctt cac tat gcg gta ttc tgc agc aac tgg 960
Gln Glu Ser Phe Ala Glu Leu His Tyr Ala Val Phe Cys Ser Asn Trp

305	310	315	320	
gtg gat caa agt gcc agc tat cgt ggg cac atg ctc atc ctg gcg gag				1008
Val Asp Gln Ser Ala Ser Tyr Arg Gly His Met Leu Ile Leu Ala Glu				
325		330	335	
cgc act aag cgg atg cag ctt ctc ctc gcc ggc aac ctg gtg ccc atc				1056
Arg Thr Lys Arg Met Gln Leu Leu Leu Ala Gly Asn Leu Val Pro Ile				
340		345	350	
cac ctg agc acc tac gtg gcc tgt tgg aag gga gcc tac tcc ttc ttc				1104
His Leu Ser Thr Tyr Val Ala Cys Trp Lys Gly Ala Tyr Ser Phe Phe				
355		360	365	
acc ctg atg gcc gat cga gat ggc ctg ggt tct tag				1140
Thr Leu Met Ala Asp Arg Asp Gly Leu Gly Ser				
370		375		

<210> 6
 <211> 379
 <212> PRT
 <213> Drosophila melanogaster

<400> 6
 Met Lys Leu Ser Glu Thr Leu Lys Ile Asp Tyr Phe Arg Val Gln Leu
 1 5 10 15
 Asn Ala Trp Arg Ile Cys Gly Ala Leu Asp Leu Ser Glu Gly Arg Tyr
 20 25 30
 Trp Ser Trp Ser Met Leu Leu Cys Ile Leu Val Tyr Leu Pro Thr Pro
 35 40 45
 Met Leu Leu Arg Gly Val Tyr Ser Phe Glu Asp Pro Val Glu Asn Asn
 50 55 60
 Phe Ser Leu Ser Leu Thr Val Thr Ser Leu Ser Asn Leu Met Lys Phe
 65 70 75 80
 Cys Met Tyr Val Ala Gln Leu Thr Lys Met Val Glu Val Gln Ser Leu
 85 90 95
 Ile Gly Gln Leu Asp Ala Arg Val Ser Gly Glu Ser Gln Ser Glu Arg
 100 105 110
 His Arg Asn Met Thr Glu His Leu Leu Arg Met Ser Lys Leu Phe Gln
 115 120 125

Ile Thr Tyr Ala Val Val Phe Ile Ile Ala Ala Val Pro Phe Val Phe
130 135 140

Glu Thr Glu Leu Ser Leu Pro Met Pro Met Trp Phe Pro Phe Asp Trp
145 150 155 160

Lys Asn Ser Met Val Ala Tyr Ile Gly Ala Leu Val Phe Gln Glu Ile
165 170 175

Gly Tyr Val Phe Gln Ile Met Gln Cys Phe Ala Ala Asp Ser Phe Pro
180 185 190

Pro Leu Val Leu Tyr Leu Ile Ser Glu Gln Cys Gln Leu Leu Ile Leu
195 200 205

Arg Ile Ser Glu Ile Gly Tyr Gly Tyr Lys Thr Leu Glu Glu Asn Glu
210 215 220

Gln Asp Leu Val Asn Cys Ile Arg Asp Gln Asn Ala Leu Tyr Arg Leu
225 230 235 240

Leu Asp Val Thr Lys Ser Leu Val Ser Tyr Pro Met Met Val Gln Phe
245 250 255

Met Val Ile Gly Ile Asn Ile Ala Ile Thr Leu Phe Val Leu Ile Phe
260 265 270

Tyr Val Glu Thr Leu Tyr Asp Arg Ile Tyr Tyr Leu Cys Phe Leu Leu
275 280 285

Gly Ile Thr Val Gln Thr Tyr Pro Leu Cys Tyr Tyr Gly Thr Met Val
290 295 300

Gln Glu Ser Phe Ala Glu Leu His Tyr Ala Val Phe Cys Ser Asn Trp
305 310 315 320

Val Asp Gln Ser Ala Ser Tyr Arg Gly His Met Leu Ile Leu Ala Glu
325 330 335

Arg Thr Lys Arg Met Gln Leu Leu Leu Ala Gly Asn Leu Val Pro Ile
340 345 350

His Leu Ser Thr Tyr Val Ala Cys Trp Lys Gly Ala Tyr Ser Phe Phe
355 360 365

Thr Leu Met Ala Asp Arg Asp Gly Leu Gly Ser
370 375

<210> 7
 <211> 1143
 <212> DNA
 <213> *Drosophila melanogaster*

 <220>
 <221> CDS
 <222> (1)..(1140)
 <223> DOR 24D.1, a coding region on BDGP Clone No.
 AC004371

<400> 7
 atg tta cct cga ttc ctg acc gcc tcc tat cca atg gag cgc cat tat 48
 Met Leu Pro Arg Phe Leu Thr Ala Ser Tyr Pro Met Glu Arg His Tyr
 1 5 10 15

 ttc atg gtg cca aag ttt gca tta tgg ctg att ggt ttt tat ccc gaa 96
 Phe Met Val Pro Lys Phe Ala Leu Ser Leu Ile Gly Phe Tyr Pro Glu
 20 25 30

 cag aag cga acg gtt ttg gtg aaa ctt tgg agt ttc ttc aac ttt ttc 144
 Gln Lys Arg Thr Val Leu Val Lys Leu Trp Ser Phe Phe Asn Phe Phe
 35 40 45

 atc ctc acc tac ggc tgt tat gca gag gct tac tat ggc ata cac tat 192
 Ile Leu Thr Tyr Gly Cys Tyr Ala Glu Ala Tyr Tyr Gly Ile His Tyr
 50 55 60

 ata ccg att aac ata gcc act gca ttg gat gcc ctt tgt oct gtg gcc 240
 Ile Pro Ile Asn Ile Ala Thr Ala Leu Asp Ala Leu Cys Pro Val Ala
 65 70 75 80

 tcc agc att ttg tgg ctg gtg aaa atg gtc gcc att tgg tgg tat caa 288
 Ser Ser Ile Leu Ser Leu Val Lys Met Val Ala Ile Trp Trp Tyr Gln
 85 90 95

 gat gaa tta agg agt ttg ata gag cgg agg ttc tat aca ctg gca acg 336
 Asp Glu Leu Arg Ser Leu Ile Glu Arg Arg Phe Tyr Thr Leu Ala Thr
 100 105 110

 caa cta aca ttc ctg cta cta tgc tgt gga ttt tgc acc agt act tcc 384
 Gln Leu Thr Phe Leu Leu Leu Cys Cys Gly Phe Cys Thr Ser Thr Ser
 115 120 125

 tat tcc gtc aga cat ttg att gat aat atc ctg aga cgc acc cat ggc 432

Tyr Ser Val Arg His Leu Ile Asp Asn Ile Leu Arg Arg Thr His Gly
 130 135 140

aag gac tgg atc tac gag act ccg ttc aag atg atg ttc ccc gat ctt 480
 Lys Asp Trp Ile Tyr Glu Thr Pro Phe Lys Met Met Phe Pro Asp Leu
 145 150 155 160

ctc ctg cgt ttg cca ctc tat ccc atc acc tat ata ctc gtg cat tgg 528
 Leu Leu Arg Leu Pro Leu Tyr Pro Ile Thr Tyr Ile Leu Val His Trp
 165 170 175

cat ggc tac att act gtg gtt tgt ttt gtc ggc gcg gat ggt ttc ttc 576
 His Gly Tyr Ile Thr Val Val Cys Phe Val Gly Ala Asp Gly Phe Phe
 180 185 190

ctg ggg ttc tgt ttg tac ttc act gtt ttg ctg ctc tgt ctg cag gac 624
 Leu Gly Phe Cys Leu Tyr Phe Thr Val Leu Leu Leu Cys Leu Gln Asp
 195 200 205

gat gtt tgt gat tta cta gag gtt gaa aac atc gag aag agt ccc tcc 672
 Asp Val Cys Asp Leu Leu Glu Val Glu Asn Ile Glu Lys Ser Pro Ser
 210 215 220

gaa gcg gag gaa gct cgc ata gtt cgg gaa atg gaa aaa ctg gtg gac 720
 Glu Ala Glu Glu Ala Arg Ile Val Arg Glu Met Glu Lys Leu Val Asp
 225 230 235 240

cgg cat aac gag gtg gcc gag ctg aca gaa aga ttg tcg ggt gtt atg 768
 Arg His Asn Glu Val Ala Glu Leu Thr Glu Arg Leu Ser Gly Val Met
 245 250 255

gtg gaa ata aca ctg gcc cac ttt gtt act tcg agt ttg ata atc gga 816
 Val Glu Ile Thr Leu Ala His Phe Val Thr Ser Ser Leu Ile Ile Gly
 260 265 270

acc agc gtg gtg gat att tta tta ttt tcc ggc ctg gga atc att gtg 864
 Thr Ser Val Val Asp Ile Leu Leu Phe Ser Gly Leu Gly Ile Ile Val
 275 280 285

tat gtg gtc tac act tgt gcc gta ggt gtg gaa ata ttt cta tac tgt 912
 Tyr Val Val Tyr Thr Cys Ala Val Gly Val Glu Ile Phe Leu Tyr Cys
 290 295 300

tta gga gga tct cat att atg gaa gcg tgt tcc aat cta gcg cgc tcc 960
 Leu Gly Gly Ser His Ile Met Glu Ala Cys Ser Asn Leu Ala Arg Ser
 305 310 315 320

aca ttt tcc agc cac tgg tat ggc cac agt gtt cgg gtc caa aag atg 1008

<210> 9
 <211> 1212
 <212> DNA
 <213> Drosophila melanogaster

<220>
 <221> CDS
 <222> (1)..(1209)

<400> 9
 atg ttc gga cac ttt aag ctc gtc tat ccg gct cct ata tcg gag ccc 48
 Met Phe Gly His Phe Lys Leu Val Tyr Pro Ala Pro Ile Ser Glu Pro
 1 5 10 15
 ata cag tct agg gat tcg aat gca tac atg atg gag acg ctg cga aat 96
 Ile Gln Ser Arg Asp Ser Asn Ala Tyr Met Met Glu Thr Leu Arg Asn
 20 25 30
 tcg ggc ttg aat ttg aag aac gat ttc ggt ata ggc cgc aag att tgg 144
 Ser Gly Leu Asn Leu Lys Asn Asp Phe Gly Ile Gly Arg Lys Ile Trp
 35 40 45
 agg gtg ttt tcg ttc acc tac aat atg gtg ata ctt ccc gta agt ttc 192
 Arg Val Phe Ser Phe Thr Tyr Asn Met Val Ile Leu Pro Val Ser Phe
 50 55 60
 cca atc aac tat gtg ata cat ctg gcg gag ttc ccg ccg gag ctg ctg 240
 Pro Ile Asn Tyr Val Ile His Leu Ala Glu Phe Pro Pro Glu Leu Leu
 65 70 75 80
 ctg caa tcc ctg caa ctg tgc ctc aac act tgg tgc ttc gct ctg aag 288
 Leu Gln Ser Leu Gln Leu Cys Leu Asn Thr Trp Cys Phe Ala Leu Lys
 85 90 95
 ttc ttc act ctg atc gtc tat acg cac cgc ttg gag ctg gcc aac aag 336
 Phe Phe Thr Leu Ile Val Tyr Thr His Arg Leu Glu Leu Ala Asn Lys
 100 105 110
 cac ttt gac gaa ttg gat aag tac tgc gtg aag ccg gcg gag aag cgc 384
 His Phe Asp Glu Leu Asp Lys Tyr Cys Val Lys Pro Ala Glu Lys Arg
 115 120 125
 aag gtt cgc gac atg gtg gcc act att aca aga ctg tac ctg acc ttc 432
 Lys Val Arg Asp Met Val Ala Thr Ile Thr Arg Leu Tyr Leu Thr Phe
 130 135 140
 gtc gtg gtc tac gtc ctc tac gcc acc tcc acg cta ctg gac gga cta 480
 Val Val Val Tyr Val Leu Tyr Ala Thr Ser Thr Leu Leu Asp Gly Leu

145	150	155	160	
ctg cac cac cgt gtt ccc tac aat acg tac tat ccg ttc ata aac tgg				528
Leu His His Arg Val Pro Tyr Asn Thr Tyr Tyr Pro Phe Ile Asn Trp				
165		170	175	
cga gtc gat cgg acc cag atg tac atc cag agt ttt ctg gag tac ttc				576
Arg Val Asp Arg Thr Gln Met Tyr Ile Gln Ser Phe Leu Glu Tyr Phe				
180		185	190	
acc gtg ggt tat gcc ata tat gtg gcc acc gcc acc gat tcc tac cct				624
Thr Val Gly Tyr Ala Ile Tyr Val Ala Thr Ala Thr Asp Ser Tyr Pro				
195		200	205	
gtg att tac gtg gca gcc ctg cga act cat att ctc ttg ctc aag gac				672
Val Ile Tyr Val Ala Ala Leu Arg Thr His Ile Leu Leu Leu Lys Asp				
210		215	220	
cgt atc att tac ttg ggc gat ccc agc aac gag ggt agc agc gac ccg				720
Arg Ile Ile Tyr Leu Gly Asp Pro Ser Asn Glu Gly Ser Ser Asp Pro				
225		230	235	240
agc tac atg ttt aaa tcg ttg gtg gat tgt atc aag gca cac aga acc				768
Ser Tyr Met Phe Lys Ser Leu Val Asp Cys Ile Lys Ala His Arg Thr				
245		250	255	
atg cta aat ttt tgt gat gcc att caa cca atc atc tct ggc acg ata				816
Met Leu Asn Phe Cys Asp Ala Ile Gln Pro Ile Ile Ser Gly Thr Ile				
260		265	270	
ttt gcc caa ttc atc ata tgc gga tcg atc ctg ggc ata att atg atc				864
Phe Ala Gln Phe Ile Ile Cys Gly Ser Ile Leu Gly Ile Ile Met Ile				
275		280	285	
aac atg gta ttg ttc gct gat caa tcg acc cga ttc ggc ata gtc atc				912
Asn Met Val Leu Phe Ala Asp Gln Ser Thr Arg Phe Gly Ile Val Ile				
290		295	300	
tac gtt atg gcc gtc ctt ctg cag act ttt ccg ctt tgc ttc tac tgc				960
Tyr Val Met Ala Val Leu Leu Gln Thr Phe Pro Leu Cys Phe Tyr Cys				
305		310	315	320
aac gcc atc gtg gac gac tgc aaa gaa ctg gcc cac gca ctt ttc cat				1008
Asn Ala Ile Val Asp Asp Cys Lys Glu Leu Ala His Ala Leu Phe His				
325		330	335	
tcc gcc tgg tgg gtg cag gac aag cga tac cag cgg act gtc atc cag				1056
Ser Ala Trp Trp Val Gln Asp Lys Arg Tyr Gln Arg Thr Val Ile Gln				

340	345	350	
ttc ctg cag aaa ctg cag cag ccc atg acc ttc acc gcc atg aac ata	1104		
Phe Leu Gln Lys Leu Gln Gln Pro Met Thr Phe Thr Ala Met Asn Ile			
355	360	365	
ttt aac att aat ttg gcc act aac atc aat gta gcc aag ttc gcc ttc	1152		
Phe Asn Ile Asn Leu Ala Thr Asn Ile Asn Val Ala Lys Phe Ala Phe			
370	375	380	
acc gtg tac gcc atc gcg agc ggt atg aac ctg gac caa aag tta agc	1200		
Thr Val Tyr Ala Ile Ala Ser Gly Met Asn Leu Asp Gln Lys Leu Ser			
385	390	395	400
att aag gaa tag			1212
Ile Lys Glu			

<210> 10
 <211> 403
 <212> PRT
 <213> Drosophila melanogaster

<400> 10
 Met Phe Gly His Phe Lys Leu Val Tyr Pro Ala Pro Ile Ser Glu Pro
 1 5 10 15
 Ile Gln Ser Arg Asp Ser Asn Ala Tyr Met Met Glu Thr Leu Arg Asn
 20 25 30
 Ser Gly Leu Asn Leu Lys Asn Asp Phe Gly Ile Gly Arg Lys Ile Trp
 35 40 45
 Arg Val Phe Ser Phe Thr Tyr Asn Met Val Ile Leu Pro Val Ser Phe
 50 55 60
 Pro Ile Asn Tyr Val Ile His Leu Ala Glu Phe Pro Pro Glu Leu Leu
 65 70 75 80
 Leu Gln Ser Leu Gln Leu Cys Leu Asn Thr Trp Cys Phe Ala Leu Lys
 85 90 95
 Phe Phe Thr Leu Ile Val Tyr Thr His Arg Leu Glu Leu Ala Asn Lys
 100 105 110
 His Phe Asp Glu Leu Asp Lys Tyr Cys Val Lys Pro Ala Glu Lys Arg
 115 120 125

Lys Val Arg Asp Met Val Ala Thr Ile Thr Arg Leu Tyr Leu Thr Phe
 130 135 140
 Val Val Val Tyr Val Leu Tyr Ala Thr Ser Thr Leu Leu Asp Gly Leu
 145 150 155 160
 Leu His His Arg Val Pro Tyr Asn Thr Tyr Tyr Pro Phe Ile Asn Trp
 165 170 175
 Arg Val Asp Arg Thr Gln Met Tyr Ile Gln Ser Phe Leu Glu Tyr Phe
 180 185 190
 Thr Val Gly Tyr Ala Ile Tyr Val Ala Thr Ala Thr Asp Ser Tyr Pro
 195 200 205
 Val Ile Tyr Val Ala Ala Leu Arg Thr His Ile Leu Leu Leu Lys Asp
 210 215 220
 Arg Ile Ile Tyr Leu Gly Asp Pro Ser Asn Glu Gly Ser Ser Asp Pro
 225 230 235 240
 Ser Tyr Met Phe Lys Ser Leu Val Asp Cys Ile Lys Ala His Arg Thr
 245 250 255
 Met Leu Asn Phe Cys Asp Ala Ile Gln Pro Ile Ile Ser Gly Thr Ile
 260 265 270
 Phe Ala Gln Phe Ile Ile Cys Gly Ser Ile Leu Gly Ile Ile Met Ile
 275 280 285
 Asn Met Val Leu Phe Ala Asp Gln Ser Thr Arg Phe Gly Ile Val Ile
 290 295 300
 Tyr Val Met Ala Val Leu Leu Gln Thr Phe Pro Leu Cys Phe Tyr Cys
 305 310 315 320
 Asn Ala Ile Val Asp Asp Cys Lys Glu Leu Ala His Ala Leu Phe His
 325 330 335
 Ser Ala Trp Trp Val Gln Asp Lys Arg Tyr Gln Arg Thr Val Ile Gln
 340 345 350
 Phe Leu Gln Lys Leu Gln Gln Pro Met Thr Phe Thr Ala Met Asn Ile
 355 360 365
 Phe Asn Ile Asn Leu Ala Thr Asn Ile Asn Val Ala Lys Phe Ala Phe
 370 375 380

Thr Val Tyr Ala Ile Ala Ser Gly Met Asn Leu Asp Gln Lys Leu Ser
 385 390 395 400

Ile Lys Glu

<210> 11

<211> 1137

<212> DNA

<213> Drosophila melanogaster

<220>

<221> CDS

<222> (1)..(1134)

<223> DOR 33B.1, a coding region on BDGP Clone No.
 AC006240

<400> 11

atg gat tca aga agg aaa gtc cga agt gaa aat ctt tac aaa acc tat 48
 Met Asp Ser Arg Arg Lys Val Arg Ser Glu Asn Leu Tyr Lys Thr Tyr
 1 5 10 15

tgg ctt tac tgg cga ctt ctg gga gtc gag ggc gat tat cct ttt cga 96
 Trp Leu Tyr Trp Arg Leu Leu Gly Val Glu Gly Asp Tyr Pro Phe Arg
 20 25 30

cgg cta gtg gat ttt aca atc acg tct ttc att acg att tta ttt ccc 144
 Arg Leu Val Asp Phe Thr Ile Thr Ser Phe Ile Thr Ile Leu Phe Pro
 35 40 45

gtg cat ctt ata ctg gga atg tat aaa aag ccc cag att caa gtc ttc 192
 Val His Leu Ile Leu Gly Met Tyr Lys Lys Pro Gln Ile Gln Val Phe
 50 55 60

agg agt ctg cat ttc aca tcg gaa tgc ctt ttc tgc agc tat aag ttt 240
 Arg Ser Leu His Phe Thr Ser Glu Cys Leu Phe Cys Ser Tyr Lys Phe
 65 70 75 80

ttc tgt ttt cgt tgg aaa ctt aaa gaa ata aag acc atc gaa gga ttg 288
 Phe Cys Phe Arg Trp Lys Leu Lys Glu Ile Lys Thr Ile Glu Gly Leu
 85 90 95

ctc cag gat ctc gat agt cga gtt gaa agt gaa gaa gaa cgc aac tac 336
 Leu Gln Asp Leu Asp Ser Arg Val Glu Ser Glu Glu Glu Arg Asn Tyr
 100 105 110

Phe Asn Gln Asn Pro Ser Arg Val Ala Arg Met Leu Ser Lys Ser Tyr
115 120 125

Leu Val Ala Ala Ile Ser Ala Ile Ile Thr Ala Thr Val Ala Gly Leu
130 135 140

Phe Ser Thr Gly Arg Asn Leu Met Tyr Leu Gly Trp Phe Pro Tyr Asp
145 150 155 160

Phe Gln Ala Thr Ala Ala Ile Tyr Trp Ile Ser Phe Ser Tyr Gln Ala
165 170 175

Ile Gly Ser Ser Leu Leu Ile Leu Glu Asn Leu Ala Asn Asp Ser Tyr
180 185 190

Pro Pro Ile Thr Phe Cys Val Val Ser Gly His Val Arg Leu Leu Ile
195 200 205

Met Arg Leu Ser Arg Ile Gly His Asp Val Lys Leu Ser Ser Ser Glu
210 215 220

Asn Thr Arg Lys Leu Ile Glu Gly Ile Gln Asp His Arg Lys Leu Met
225 230 235 240

Lys Ile Ile Arg Leu Leu Arg Ser Thr Leu His Leu Ser Gln Leu Gly
245 250 255

Gln Phe Leu Ser Ser Gly Ile Asn Ile Ser Ile Thr Leu Ile Asn Ile
260 265 270

Leu Phe Phe Ala Glu Asn Asn Phe Ala Met Leu Tyr Tyr Ala Val Phe
275 280 285

Phe Ala Ala Met Leu Ile Glu Leu Phe Pro Ser Cys Tyr Tyr Gly Ile
290 295 300

Leu Met Thr Met Glu Phe Asp Lys Leu Pro Tyr Ala Ile Phe Ser Ser
305 310 315 320

Asn Trp Leu Lys Met Asp Lys Arg Tyr Asn Arg Ser Leu Ile Ile Leu
325 330 335

Met Gln Leu Thr Leu Val Pro Val Asn Ile Lys Ala Gly Gly Ile Val
340 345 350

Gly Ile Asp Met Ser Ala Phe Phe Ala Thr Val Arg Met Ala Tyr Ser
355 360 365

Phe Tyr Thr Leu Ala Leu Ser Phe Arg Val
 370 375

<210> 13
 <211> 1140
 <212> DNA
 <213> Drosophila melanogaster

<220>
 <221> CDS
 <222> (1)..(1137)
 <223> DOR 33B.2, a coding region on BDGP Clone No.
 AC006240

<400> 13
 atg gac tta aaa ccg cga gtc att cga agt gaa gat atc tac aga acc 48
 Met Asp Leu Lys Pro Arg Val Ile Arg Ser Glu Asp Ile Tyr Arg Thr
 1 5 10 15
 tat tgg tta tat tgg cat ctt ttg ggc ctg gaa agc aat ttc ttt ctg 96
 Tyr Trp Leu Tyr Trp His Leu Leu Gly Leu Glu Ser Asn Phe Phe Leu
 20 25 30
 aat cgc ttg ttg gat ttg gtg att aca att ttc gta acc att tgg tat 144
 Asn Arg Leu Leu Asp Leu Val Ile Thr Ile Phe Val Thr Ile Trp Tyr
 35 40 45
 cca att cac ctg att ctg gga ctg ttt atg gaa aga tot ttg ggg gat 192
 Pro Ile His Leu Ile Leu Gly Leu Phe Met Glu Arg Ser Leu Gly Asp
 50 55 60
 gtc tgc aag ggt cta cca att acg gca gca tgc ttt ttc gcc agc ttt 240
 Val Cys Lys Gly Leu Pro Ile Thr Ala Ala Cys Phe Phe Ala Ser Phe
 65 70 75 80
 aaa ttt att tgt ttt cgc ttc aag cta tct gaa att aaa gaa atc gaa 288
 Lys Phe Ile Cys Phe Arg Phe Lys Leu Ser Glu Ile Lys Glu Ile Glu
 85 90 95
 ata tta ttt aaa gag ctg gat cag cga gct tta agt cga gag gaa tgc 336
 Ile Leu Phe Lys Glu Leu Asp Gln Arg Ala Leu Ser Arg Glu Glu Cys
 100 105 110
 gag ttt ttc aat caa aat acg aga cgt gag gcg aat ttc att tgg aaa 384
 Glu Phe Phe Asn Gln Asn Thr Arg Arg Glu Ala Asn Phe Ile Trp Lys
 115 120 125

Ser Phe Ile Val Ala Tyr Gly Leu Ser Asn Ile Ser Ala Ile Ala Ser
130 135 140

Val Leu Phe Gly Gly Gly His Lys Leu Leu Tyr Pro Ala Trp Phe Pro
145 150 155 160

Tyr Asp Val Gln Ala Thr Glu Leu Ile Phe Trp Leu Ser Val Thr Tyr
165 170 175

Gln Ile Ala Gly Val Ser Leu Ala Ile Leu Gln Asn Leu Ala Asn Asp
180 185 190

Ser Tyr Pro Pro Met Thr Phe Cys Val Val Ala Gly His Val Arg Leu
195 200 205

Leu Ala Met Arg Leu Ser Arg Ile Gly Gln Gly Pro Glu Glu Thr Ile
210 215 220

Tyr Leu Thr Gly Lys Gln Leu Ile Glu Ser Ile Glu Asp His Arg Lys
225 230 235 240

Leu Met Lys Ile Val Glu Leu Leu Arg Ser Thr Met Asn Ile Ser Gln
245 250 255

Leu Gly Gln Phe Ile Ser Ser Gly Val Asn Ile Ser Ile Thr Leu Val
260 265 270

Asn Ile Leu Phe Phe Ala Asp Asn Asn Phe Ala Ile Thr Tyr Tyr Gly
275 280 285

Val Tyr Phe Leu Ser Met Val Leu Glu Leu Phe Pro Cys Cys Tyr Tyr
290 295 300

Gly Thr Leu Ile Ser Val Glu Met Asn Gln Leu Thr Tyr Ala Ile Tyr
305 310 315 320

Ser Ser Asn Trp Met Ser Met Asn Arg Ser Tyr Ser Arg Ile Leu Leu
325 330 335

Ile Phe Met Gln Leu Thr Leu Ala Glu Val Gln Ile Lys Ala Gly Gly
340 345 350

Met Ile Gly Ile Gly Met Asn Ala Phe Phe Ala Thr Val Arg Leu Ala
355 360 365

Tyr Ser Phe Phe Thr Leu Ala Met Ser Leu Arg
370 375

<210> 15
 <211> 1155
 <212> DNA
 <213> Drosophila melanogaster

<220>
 <221> CDS
 <222> (1)..(1152)
 <223> DOR 33B3.3, a coding region on BDGP Clone No.
 AC006240

<400> 15
 atg gtc att atc gac agt ctt agt ttt tat cgt cca ttc tgg atc tgc 48
 Met Val Ile Ile Asp Ser Leu Ser Phe Tyr Arg Pro Phe Trp Ile Cys
 1 5 10 15

atg cga ttg ctg gta ccg act ttc ttc aag gat tcc tca cgt cct gtc 96
 Met Arg Leu Leu Val Pro Thr Phe Phe Lys Asp Ser Ser Arg Pro Val
 20 25 30

cag ctg tac gtg gtg ttg ctg cac atc ctg gtc acc ttg tgg ttt cca 144
 Gln Leu Tyr Val Val Leu Leu His Ile Leu Val Thr Leu Trp Phe Pro
 35 40 45

ctg cat ctg ctg ctg cat ctt ctg cta ctt cca tct acc gct gag ttc 192
 Leu His Leu Leu Leu His Leu Leu Leu Leu Pro Ser Thr Ala Glu Phe
 50 55 60

ttt aag aac ctg acc atg tct ctg act tgt gtg gcc tgc agt ctg aag 240
 Phe Lys Asn Leu Thr Met Ser Leu Thr Cys Val Ala Cys Ser Leu Lys
 65 70 75 80

cat gtg gcc cac ttg tat cac ttg ccg cag att gtg gaa atc gaa tca 288
 His Val Ala His Leu Tyr His Leu Pro Gln Ile Val Glu Ile Glu Ser
 85 90 95

ctg atc gag caa tta gac aca ttt att gcc agc gaa cag gag cat cgt 336
 Leu Ile Glu Gln Leu Asp Thr Phe Ile Ala Ser Glu Gln Glu His Arg
 100 105 110

tac tat cgg gat cac gta cat tgc cat gct agg cgc ttt aca aga tgt 384
 Tyr Tyr Arg Asp His Val His Cys His Ala Arg Arg Phe Thr Arg Cys
 115 120 125

ctc tat att agc ttt ggc atg atc tat gcg ctt ttc ctg ttc ggc gtc 432
 Leu Tyr Ile Ser Phe Gly Met Ile Tyr Ala Leu Phe Leu Phe Gly Val

130	135	140	
ttc gtt cag gtt att agc gga aat tgg gaa ctt ctc tat cca gcc tat			480
Phe Val Gln Val Ile Ser Gly Asn Trp Glu Leu Leu Tyr Pro Ala Tyr			
145	150	155	160
ttc cca ttc gac ttg gag agc aat cgc ttt ctc ggc gca gta gcc ttg			528
Phe Pro Phe Asp Leu Glu Ser Asn Arg Phe Leu Gly Ala Val Ala Leu			
165	170	175	
ggc tat cag gta ttc agc atg tta gtt gaa ggc ttc cag ggg ctg ggc			576
Gly Tyr Gln Val Phe Ser Met Leu Val Glu Gly Phe Gln Gly Leu Gly			
180	185	190	
aac gat acc tat acc cca ctg acc cta tgc ctt ctg gcc gga cat gtc			624
Asn Asp Thr Tyr Thr Pro Leu Thr Leu Cys Leu Leu Ala Gly His Val			
195	200	205	
cat ttg tgg tcc ata cga atg ggt caa ctg gga tac ttc gat gac gag			672
His Leu Trp Ser Ile Arg Met Gly Gln Leu Gly Tyr Phe Asp Asp Glu			
210	215	220	
acg gtg gtg aat cat cag cgt ttg ctg gat tac att gag cag cat aaa			720
Thr Val Val Asn His Gln Arg Leu Leu Asp Tyr Ile Glu Gln His Lys			
225	230	235	240
ctc ttg gtg cga ttc cac aac ctg gtg agc cgg acc atc agc gaa gtg			768
Leu Leu Val Arg Phe His Asn Leu Val Ser Arg Thr Ile Ser Glu Val			
245	250	255	
caa ctg gtg cag ctg ggc gga tgt gga gcc act ctg tgc atc att gtc			816
Gln Leu Val Gln Leu Gly Gly Cys Gly Ala Thr Leu Cys Ile Ile Val			
260	265	270	
tcc tac atg ctc ttc ttt gtg ggc gac aca atc tcg ctg gtc tac tac			864
Ser Tyr Met Leu Phe Phe Val Gly Asp Thr Ile Ser Leu Val Tyr Tyr			
275	280	285	
ttg gtg ttc ttt gga gtg gtc tgc gtg cag ctc ttt ccc agc tgc tat			912
Leu Val Phe Phe Gly Val Val Cys Val Gln Leu Phe Pro Ser Cys Tyr			
290	295	300	
ttt gcc agc gaa gta gcc gag gag ttg gaa cgg ctg cca tat gcg atc			960
Phe Ala Ser Glu Val Ala Glu Glu Leu Glu Arg Leu Pro Tyr Ala Ile			
305	310	315	320
ttc tcc agc aga tgg tac gat caa tcg cgg gat cat cga ttc gat ttg			1008
Phe Ser Ser Arg Trp Tyr Asp Gln Ser Arg Asp His Arg Phe Asp Leu			

325	330	335	
ctc atc ttt aca caa tta aca ctg gga aac cgg ggg tgg atc atc aag	1056		
Leu Ile Phe Thr Gln Leu Thr Leu Gly Asn Arg Gly Trp Ile Ile Lys			
340	345	350	
gca gga ggt ctt atc gag ctg aat ttg aat gcc ttt ttc gcc acc ctg	1104		
Ala Gly Gly Leu Ile Glu Leu Asn Leu Asn Ala Phe Phe Ala Thr Leu			
355	360	365	
aag atg gcc tat tcc ctt ttt gca gtt gtg gtg cgg gca aag ggt ata	1152		
Lys Met Ala Tyr Ser Leu Phe Ala Val Val Val Arg Ala Lys Gly Ile			
370	375	380	
tag			1155
<210> 16			
<211> 384			
<212> PRT			
<213> Drosophila melanogaster			
<400> 16			
Met Val Ile Ile Asp Ser Leu Ser Phe Tyr Arg Pro Phe Trp Ile Cys			
1	5	10	15
Met Arg Leu Leu Val Pro Thr Phe Phe Lys Asp Ser Ser Arg Pro Val			
20	25	30	
Gln Leu Tyr Val Val Leu Leu His Ile Leu Val Thr Leu Trp Phe Pro			
35	40	45	
Leu His Leu Leu Leu His Leu Leu Leu Leu Pro Ser Thr Ala Glu Phe			
50	55	60	
Phe Lys Asn Leu Thr Met Ser Leu Thr Cys Val Ala Cys Ser Leu Lys			
65	70	75	80
His Val Ala His Leu Tyr His Leu Pro Gln Ile Val Glu Ile Glu Ser			
85	90	95	
Leu Ile Glu Gln Leu Asp Thr Phe Ile Ala Ser Glu Gln Glu His Arg			
100	105	110	
Tyr Tyr Arg Asp His Val His Cys His Ala Arg Arg Phe Thr Arg Cys			
115	120	125	
Leu Tyr Ile Ser Phe Gly Met Ile Tyr Ala Leu Phe Leu Phe Gly Val			

130

135

140

Phe Val Gln Val Ile Ser Gly Asn Trp Glu Leu Leu Tyr Pro Ala Tyr
145 150 155 160

Phe Pro Phe Asp Leu Glu Ser Asn Arg Phe Leu Gly Ala Val Ala Leu
165 170 175

Gly Tyr Gln Val Phe Ser Met Leu Val Glu Gly Phe Gln Gly Leu Gly
180 185 190

Asn Asp Thr Tyr Thr Pro Leu Thr Leu Cys Leu Leu Ala Gly His Val
195 200 205

His Leu Trp Ser Ile Arg Met Gly Gln Leu Gly Tyr Phe Asp Asp Glu
210 215 220

Thr Val Val Asn His Gln Arg Leu Leu Asp Tyr Ile Glu Gln His Lys
225 230 235 240

Leu Leu Val Arg Phe His Asn Leu Val Ser Arg Thr Ile Ser Glu Val
245 250 255

Gln Leu Val Gln Leu Gly Gly Cys Gly Ala Thr Leu Cys Ile Ile Val
260 265 270

Ser Tyr Met Leu Phe Phe Val Gly Asp Thr Ile Ser Leu Val Tyr Tyr
275 280 285

Leu Val Phe Phe Gly Val Val Cys Val Gln Leu Phe Pro Ser Cys Tyr
290 295 300

Phe Ala Ser Glu Val Ala Glu Glu Leu Glu Arg Leu Pro Tyr Ala Ile
305 310 315 320

Phe Ser Ser Arg Trp Tyr Asp Gln Ser Arg Asp His Arg Phe Asp Leu
325 330 335

Leu Ile Phe Thr Gln Leu Thr Leu Gly Asn Arg Gly Trp Ile Ile Lys
340 345 350

Ala Gly Gly Leu Ile Glu Leu Asn Leu Asn Ala Phe Phe Ala Thr Leu
355 360 365

Lys Met Ala Tyr Ser Leu Phe Ala Val Val Val Arg Ala Lys Gly Ile
370 375 380

<210> 17
 <211> 1152
 <212> DNA
 <213> Drosophila melanogaster

<220>
 <221> CDS
 <222> (1)..(1149)
 <223> DOR 43B.1, coding region of AF127926

<400> 17
 atg aca atc gag gat atc ggc ctg gtg ggc atc aac gtg cgg atg tgg 48
 Met Thr Ile Glu Asp Ile Gly Leu Val Gly Ile Asn Val Arg Met Trp
 1 5 10 15
 cga cac ttg gcc gtg ctg tac ccc act ccg ggc tcc agc tgg cgc aag 96
 Arg His Leu Ala Val Leu Tyr Pro Thr Pro Gly Ser Ser Trp Arg Lys
 20 25 30
 ttc gcc ttc gtg ctg ccg gtg act gcg atg aat ctg atg cag ttc gtc 144
 Phe Ala Phe Val Leu Pro Val Thr Ala Met Asn Leu Met Gln Phe Val
 35 40 45
 tac ctg ctg cgg atg tgg ggc gac ctg ccc gcc ttc att ctg aac atg 192
 Tyr Leu Leu Arg Met Trp Gly Asp Leu Pro Ala Phe Ile Leu Asn Met
 50 55 60
 ttc ttc ttc tcg gcc att ttc aac gcc ctg atg cgc acg tgg ctg gtc 240
 Phe Phe Phe Ser Ala Ile Phe Asn Ala Leu Met Arg Thr Trp Leu Val
 65 70 75 80
 ata atc aag cgg cgc cag ttc gag gag ttt ctc ggc caa ctg gcc act 288
 Ile Ile Lys Arg Arg Gln Phe Glu Glu Phe Leu Gly Gln Leu Ala Thr
 85 90 95
 ctg ttc cat tcg att ctc gac tcc acc gac gag tgg ggg cgt gcc atc 336
 Leu Phe His Ser Ile Leu Asp Ser Thr Asp Glu Trp Gly Arg Gly Ile
 100 105 110
 ctg cgg agg gcg gaa cgg gag gct cgg aac ctg gcc atc ctt aat ttg 384
 Leu Arg Arg Ala Glu Arg Glu Ala Arg Asn Leu Ala Ile Leu Asn Leu
 115 120 125
 agt gcc tcc ttc ctg gac att gtc ggt gct ctg ttt ttc gaa tat aaa 432
 Ser Ala Ser Phe Leu Asp Ile Val Gly Ala Leu Phe Phe Glu Tyr Lys
 130 135 140

ctc ctg atc ttc ttg atg caa aca caa cac ccg atg gag ata aga gtc 1056
 Leu Leu Ile Phe Leu Met Gln Thr Gln His Pro Met Glu Ile Arg Val
 340 345 350

ggc aac gtt tac ccc atg aca ttg gcc atg ttc cag agt ctg ttg aat 1104
 Gly Asn Val Tyr Pro Met Thr Leu Ala Met Phe Gln Ser Leu Leu Asn
 355 360 365

gcg tcc tac tcc tac ttt acc atg ctg cgt ggc gtc acc ggc aaa tga 1152
 Ala Ser Tyr Ser Tyr Phe Thr Met Leu Arg Gly Val Thr Gly Lys
 370 375 380

<210> 18

<211> 383

<212> PRT

<213> Drosophila melanogaster

<400> 18

Met Thr Ile Glu Asp Ile Gly Leu Val Gly Ile Asn Val Arg Met Trp
 1 5 10 15

Arg His Leu Ala Val Leu Tyr Pro Thr Pro Gly Ser Ser Trp Arg Lys
 20 25 30

Phe Ala Phe Val Leu Pro Val Thr Ala Met Asn Leu Met Gln Phe Val
 35 40 45

Tyr Leu Leu Arg Met Trp Gly Asp Leu Pro Ala Phe Ile Leu Asn Met
 50 55 60

Phe Phe Phe Ser Ala Ile Phe Asn Ala Leu Met Arg Thr Trp Leu Val
 65 70 75 80

Ile Ile Lys Arg Arg Gln Phe Glu Glu Phe Leu Gly Gln Leu Ala Thr
 85 90 95

Leu Phe His Ser Ile Leu Asp Ser Thr Asp Glu Trp Gly Arg Gly Ile
 100 105 110

Leu Arg Arg Ala Glu Arg Glu Ala Arg Asn Leu Ala Ile Leu Asn Leu
 115 120 125

Ser Ala Ser Phe Leu Asp Ile Val Gly Ala Leu Phe Phe Glu Tyr Lys
 130 135 140

Phe Pro Ile Gly Val Val Thr Phe Phe Leu Pro Ala His Pro Phe Gly
 145 150 155 160

Leu Ala Leu Pro Gly Val Ser Met Thr Ser Ser Pro Val Tyr Glu Val
165 170 175

Ile Tyr Leu Ala Gln Leu Pro Thr Pro Leu Leu Leu Ser Met Met Tyr
180 185 190

Met Pro Phe Val Ser Leu Phe Ala Gly Leu Ala Ile Phe Gly Lys Ala
195 200 205

Met Leu Gln Ile Leu Val His Arg Leu Gly Gln Ile Gly Gly Glu Glu
210 215 220

Gln Ser Glu Glu Glu Arg Phe Gln Arg Leu Ala Ser Cys Ile Ala Tyr
225 230 235 240

His Thr Gln Val Met Arg Tyr Val Trp Gln Leu Asn Lys Leu Val Ala
245 250 255

Asn Ile Val Ala Val Glu Ala Ile Ile Phe Gly Ser Ile Ile Cys Ser
260 265 270

Leu Leu Phe Cys Leu Asn Ile Ile Thr Ser Pro Thr Gln Val Ile Ser
275 280 285

Ile Val Met Tyr Ile Leu Thr Met Leu Tyr Val Leu Phe Thr Tyr Tyr
290 295 300

Asn Arg Ala Asn Glu Ile Cys Leu Glu Asn Asn Arg Val Ala Glu Ala
305 310 315 320

Val Tyr Asn Val Pro Trp Tyr Glu Ala Gly Thr Arg Phe Arg Lys Thr
325 330 335

Leu Leu Ile Phe Leu Met Gln Thr Gln His Pro Met Glu Ile Arg Val
340 345 350

Gly Asn Val Tyr Pro Met Thr Leu Ala Met Phe Gln Ser Leu Leu Asn
355 360 365

Ala Ser Tyr Ser Tyr Phe Thr Met Leu Arg Gly Val Thr Gly Lys
370 375 380

<210> 19

<211> 1158

<212> DNA

<221> CDS

<223> DOR 46F.1, a coding region on BDGP Clone No.

AC005974

atg agc aaa gga gta gaa atc ttt tac aag ggc cag aag gca ttc ttg 48
Met Ser Lys Gly Val Glu Ile Phe Tyr Lys Gly Gln Lys Ala Phe Leu
1 5 10 15

aac atc ctc tgc ttg tgg cct cag ata gaa cgc cgg tgg aga atc atc 96
Asn Ile Leu Ser Leu Trp Pro Gln Ile Glu Arg Arg Trp Arg Ile Ile
20 25 30

cac cag gtg aac tat gtc cac gta att gtg ttt tgg gtg ctg ctc ttt 144
His Gln Val Asn Tyr Val His Val Ile Val Phe Trp Val Leu Leu Phe
 35 40 45

gat ctc ctc ttg gtg ctc cat gtg atg gct aat ttg agc tac atg tcc 192
Asp Leu Leu Leu Val Leu His Val Met Ala Asn Leu Ser Tyr Met Ser
50 55 60

gag gtt gtg aaa gcc atc ttt atc ctg gcc acc agt gca ggg cac acc 240
Glu Val Val Lys Ala Ile Phe Ile Leu Ala Thr Ser Ala Gly His Thr
65 70 75 80

acc aag ctg ctg tcc ata aag gcg aac aat gtg cag atg gag gag ctc 288
Thr Lys Leu Leu Ser Ile Lys Ala Asn Asn Val Gln Met Glu Glu Leu
85 90 95

ttt agg aga ttg gat aac gaa gag ttc cgt cct aga ggc gcc aac gaa 336
Phe Arg Arg Leu Asp Asn Glu Glu Phe Arg Pro Arg Gly Ala Asn Glu
100 105 110

gag ttg atc ttt gca gca gcc tgt gaa aga agt agg aag ctt cgg gac 384
Glu Leu Ile Phe Ala Ala Ala Cys Glu Arg Ser Arg Lys Leu Arg Asp
115 120 125

ttc tat gga gcg ctt tcg ttt gcc gcc ttg agc atg att ctc ata ccc 432
Phe Tyr Gly Ala Leu Ser Phe Ala Ala Leu Ser Met Ile Leu Ile Pro
130 135 140

cag ttc gcc ttg gac tgg tcc cac ctt ccg ctc aaa aca tac aat ccg 480
Gln Phe Ala Leu Asp Trp Ser His Leu Pro Leu Lys Thr Tyr Asn Pro
145 150 155 160

005270 22515160

145	150	155	160
Leu Gly Glu Asn Thr Gly Ser Pro Ala Tyr Trp Leu Leu Tyr Cys Tyr	165	170	175
Gln Cys Leu Ala Leu Ser Val Ser Cys Ile Thr Asn Ile Gly Phe Asp	180	185	190
Ser Leu Cys Ser Ser Leu Phe Ile Phe Leu Lys Cys Gln Leu Asp Ile	195	200	205
Leu Ala Val Arg Leu Asp Lys Ile Gly Arg Leu Ile Thr Thr Ser Gly	210	215	220
Gly Thr Val Glu Gln Gln Leu Lys Glu Asn Ile Arg Tyr His Met Thr	225	230	235
Ile Val Glu Leu Ser Lys Thr Val Glu Arg Leu Leu Cys Lys Pro Ile	245	250	255
Ser Val Gln Ile Phe Cys Ser Val Leu Val Leu Thr Ala Asn Phe Tyr	260	265	270
Ala Ile Ala Val Leu Ser Asp Glu Arg Leu Glu Leu Phe Lys Tyr Val	275	280	285
Thr Tyr Gln Ala Cys Met Leu Ile Gln Ile Phe Ile Leu Cys Tyr Tyr	290	295	300
Ala Gly Glu Val Thr Gln Arg Ser Leu Asp Leu Pro His Glu Leu Tyr	305	310	315
Lys Thr Ser Trp Val Asp Trp Asp Tyr Arg Ser Arg Arg Ile Ala Leu	325	330	335
Leu Phe Met Gln Arg Leu His Ser Thr Leu Arg Ile Arg Thr Leu Asn	340	345	350
Pro Ser Leu Gly Phe Asp Leu Met Leu Phe Ser Ser Val Ser Ser Phe	355	360	365
Arg Val Leu Thr Phe Leu Cys Thr Val Ala Asn Phe His Asn Glu Ala	370	375	380
His			
385			

<210> 21
 <211> 1155
 <212> DNA
 <213> Drosophila melanogaster

<220>
 <221> CDS
 <222> (1)..(1152)
 <223> DOR 46F.2, a coding region on BDGP Clone No.
 AC005974

<400> 21
 atg gtt acg gag gac ttt tat aag tac cag gtg tgg tac ttc caa atc 48
 Met Val Thr Glu Asp Phe Tyr Lys Tyr Gln Val Trp Tyr Phe Gln Ile
 1 5 10 15
 ctt ggt gtt tgg cag ctc ccc act tgg gcc gca gac cac cag cgt cgt 96
 Leu Gly Val Trp Gln Leu Pro Thr Trp Ala Ala Asp His Gln Arg Arg
 20 25 30
 ttt cag tcc atg agg ttt ggc ttc atc ctg gtc atc ctg ttc atc atg 144
 Phe Gln Ser Met Arg Phe Gly Phe Ile Leu Val Ile Leu Phe Ile Met
 35 40 45
 ctg ctg ctt ttc tcc ttc gaa atg ttg aac aac att tcc caa gtt agg 192
 Leu Leu Leu Phe Ser Phe Glu Met Leu Asn Asn Ile Ser Gln Val Arg
 50 55 60
 gag atc cta aag gta ttc ttc atg ttc gcc acg gaa ata tcc tgc atg 240
 Glu Ile Leu Lys Val Phe Phe Met Phe Ala Thr Glu Ile Ser Cys Met
 65 70 75 80
 gcc aaa tta ttg cat ttg aag ttg aag agc cgc aaa ctc gct ggc ttg 288
 Ala Lys Leu Leu His Leu Lys Leu Lys Ser Arg Lys Leu Ala Gly Leu
 85 90 95
 gtt gat gcg atg ttg tcc cca gag ttc ggc gtt aaa agt gaa cag gaa 336
 Val Asp Ala Met Leu Ser Pro Glu Phe Gly Val Lys Ser Glu Gln Glu
 100 105 110
 atg cag atg ctg gaa ttg gat aga gtg gcg gtt gtc cgc atg agg aac 384
 Met Gln Met Leu Glu Leu Asp Arg Val Ala Val Val Arg Met Arg Asn
 115 120 125
 tcc tac ggc atc atg tcc ctg ggc gcg gct tcc ctg atc ctt ata gtt 432
 Ser Tyr Gly Ile Met Ser Leu Gly Ala Ala Ser Leu Ile Leu Ile Val
 130 135 140

<210> 23
 <211> 1158
 <212> DNA
 <213> *Drosophila melanogaster*

<220>
 <221> CDS
 <222> (1)..(1155)
 <223> DOR 47E.1, coding region of AF156880

<400> 23
 atg gac agt ttt ctg caa gta cag aag agc acc att gcc ctt ctg ggc 48
 Met Asp Ser Phe Leu Gln Val Gln Lys Ser Thr Ile Ala Leu Leu Gly
 1 5 10 15

ttt gat ctc ttt agt gaa aat cga gaa atg tgg aaa cgc ccc tat aga 96
 Phe Asp Leu Phe Ser Glu Asn Arg Glu Met Trp Lys Arg Pro Tyr Arg
 20 25 30

gca atg aat gtg ttt agc ata gct gcc att ttt ccc ttt atc ctg gca 144
 Ala Met Asn Val Phe Ser Ile Ala Ala Ile Phe Pro Phe Ile Leu Ala
 35 40 45

gct gtg ctc cat aat tgg aag aat gta ttg ctg ctg gcc gat gcc atg 192
 Ala Val Leu His Asn Trp Lys Asn Val Leu Leu Leu Ala Asp Ala Met
 50 55 60

gtg gcc cta cta ata acc att ctg ggc cta ttc aag ttt agc atg ata 240
 Val Ala Leu Leu Ile Thr Ile Leu Gly Leu Phe Lys Phe Ser Met Ile
 65 70 75 80

ctt tac tta cgt cgc gat ttc aag cga ctg att gac aaa ttt cgt ttg 288
 Leu Tyr Leu Arg Arg Asp Phe Lys Arg Leu Ile Asp Lys Phe Arg Leu
 85 90 95

ctc atg tcg aat gag gcg gaa cag ggc gag gaa tac gcc gag att ctc 336
 Leu Met Ser Asn Glu Ala Glu Gln Gly Glu Glu Tyr Ala Glu Ile Leu
 100 105 110

aac gca gca aac aag cag gat caa cga atg tgc act ctg ttt agg act 384
 Asn Ala Ala Asn Lys Gln Asp Gln Arg Met Cys Thr Leu Phe Arg Thr
 115 120 125

tgt ttc ctc ctc gcc tgg gcc ttg aat agt gtt ctg ccc ctc gtg aga 432
 Cys Phe Leu Leu Ala Trp Ala Leu Asn Ser Val Leu Pro Leu Val Arg
 130 135 140

atg ggt ctc agc tat tgg tta gca ggt cat gca gag ccc gag ttg cct 480

Met Gly Leu Ser Tyr Trp Leu Ala Gly His Ala Glu Pro Glu Leu Pro	
145	155
150	160
ttt ccc tgt ctt ttt ccc tgg aat atc cac atc att cgc aat tat gtt	528
Phe Pro Cys Leu Phe Pro Trp Asn Ile His Ile Ile Arg Asn Tyr Val	
165	175
170	
ttg agc ttc atc tgg agc gct ttc gcc tcg aca ggt gtg gtt tta cct	576
Leu Ser Phe Ile Trp Ser Ala Phe Ala Ser Thr Gly Val Val Leu Pro	
180	190
185	
gct gtc agc ttg gat acc ata ttc tgt tcc ttc acc agc aac ctg tgc	624
Ala Val Ser Leu Asp Thr Ile Phe Cys Ser Phe Thr Ser Asn Leu Cys	
195	205
200	
gcc ttc ttc aaa att gcg cag tac aag gtg gtt aga ttt aag ggc gga	672
Ala Phe Phe Lys Ile Ala Gln Tyr Lys Val Val Arg Phe Lys Gly Gly	
210	220
215	
tcc ctt aaa gaa tca cag gcc aca ttg aac aaa gtc ttt gcc ctg tac	720
Ser Leu Lys Glu Ser Gln Ala Thr Leu Asn Lys Val Phe Ala Leu Tyr	
225	235
230	240
cag acc agc ttg gat atg tgc aac gat ctg aat cag tgc tac caa ccg	768
Gln Thr Ser Leu Asp Met Cys Asn Asp Leu Asn Gln Cys Tyr Gln Pro	
245	255
250	
att atc tgc gcc cag ttc ttc att tca tct ctg caa ctc tgc atg ctg	816
Ile Ile Cys Ala Gln Phe Phe Ile Ser Ser Leu Gln Leu Cys Met Leu	
260	270
265	
gga tat ctg ttc tcc att act ttt gcc cag aca gag ggc gtc tac tat	864
Gly Tyr Leu Phe Ser Ile Thr Phe Ala Gln Thr Glu Gly Val Tyr Tyr	
275	285
280	
gcc tca ttc ata gcc aca atc att ata caa gcc tat atc tac tgc tac	912
Ala Ser Phe Ile Ala Thr Ile Ile Ile Gln Ala Tyr Ile Tyr Cys Tyr	
290	300
295	
tgc ggg gag aac ctg aag acg gag agt gcc agc ttc gag tgg gcc atc	960
Cys Gly Glu Asn Leu Lys Thr Glu Ser Ala Ser Phe Glu Trp Ala Ile	
305	315
310	320
tac gac agt ccg tgg cac gag agt ttg ggt gct ggt gga gcc tct acc	1008
Tyr Asp Ser Pro Trp His Glu Ser Leu Gly Ala Gly Gly Ala Ser Thr	
325	335
330	
tcg atc tgc cga tcc ttg ctg atc agc atg atg cgg gct cat cgg gga	1056

Met Gly Leu Ser Tyr Trp Leu Ala Gly His Ala Glu Pro Glu Leu Pro
145 150 155 160

Phe Pro Cys Leu Phe Pro Trp Asn Ile His Ile Ile Arg Asn Tyr Val
165 170 175

Leu Ser Phe Ile Trp Ser Ala Phe Ala Ser Thr Gly Val Val Leu Pro
180 185 190

Ala Val Ser Leu Asp Thr Ile Phe Cys Ser Phe Thr Ser Asn Leu Cys
195 200 205

Ala Phe Phe Lys Ile Ala Gln Tyr Lys Val Val Arg Phe Lys Gly Gly
210 215 220

Ser Leu Lys Glu Ser Gln Ala Thr Leu Asn Lys Val Phe Ala Leu Tyr
225 230 235 240

Gln Thr Ser Leu Asp Met Cys Asn Asp Leu Asn Gln Cys Tyr Gln Pro
245 250 255

Ile Ile Cys Ala Gln Phe Phe Ile Ser Ser Leu Gln Leu Cys Met Leu
260 265 270

Gly Tyr Leu Phe Ser Ile Thr Phe Ala Gln Thr Glu Gly Val Tyr Tyr
275 280 285

Ala Ser Phe Ile Ala Thr Ile Ile Ile Gln Ala Tyr Ile Tyr Cys Tyr
290 295 300

Cys Gly Glu Asn Leu Lys Thr Glu Ser Ala Ser Phe Glu Trp Ala Ile
305 310 315 320

Tyr Asp Ser Pro Trp His Glu Ser Leu Gly Ala Gly Gly Ala Ser Thr
325 330 335

Ser Ile Cys Arg Ser Leu Leu Ile Ser Met Met Arg Ala His Arg Gly
340 345 350

Phe Arg Ile Thr Gly Tyr Phe Phe Glu Ala Asn Met Glu Ala Phe Ser
355 360 365

Ser Ile Val Arg Thr Ala Met Ser Tyr Ile Thr Met Leu Arg Ser Phe
370 375 380

Ser
385

<210> 25
 <211> 1203
 <212> DNA
 <213> Drosophila melanogaster

<220>
 <221> CDS
 <222> (1)..(1200)
 <223> DOR 47E.2, a coding region on BDGP Clone No.
 AC005638

<400> 25
 atg aac gac tcg ggt tat caa tca aat ctc agc ctt ctg cgg gtt ttt 48
 Met Asn Asp Ser Gly Tyr Gln Ser Asn Leu Ser Leu Leu Arg Val Phe
 1 5 10 15

ctc gac gag ttc cga tcg gtt ctg cgg cag gaa agt ccc ggt ctc atc 96
 Leu Asp Glu Phe Arg Ser Val Leu Arg Gln Glu Ser Pro Gly Leu Ile
 20 25 30

cca cgc ctg gct ttt tac tat gtt cgc gcc ttt ctg agc ttg ccc ctg 144
 Pro Arg Leu Ala Phe Tyr Tyr Val Arg Ala Phe Leu Ser Leu Pro Leu
 35 40 45

tac cga tgg atc aac ttg ttc atc atg tgc aat gtg atg acc att ttc 192
 Tyr Arg Trp Ile Asn Leu Phe Ile Met Cys Asn Val Met Thr Ile Phe
 50 55 60

tgg acc atg ttc gtg gcc ctg ccc gag tcg aag aac gtg atc gaa atg 240
 Trp Thr Met Phe Val Ala Leu Pro Glu Ser Lys Asn Val Ile Glu Met
 65 70 75 80

ggc gac gac ttg gtt tgg att tcg ggg atg gca ctg gtg ttc acc aag 288
 Gly Asp Asp Leu Val Trp Ile Ser Gly Met Ala Leu Val Phe Thr Lys
 85 90 95

atc ttt tac atg cat ttg cgt tgc gac gag atc gat gaa ctt att tcg 336
 Ile Phe Tyr Met His Leu Arg Cys Asp Glu Ile Asp Glu Leu Ile Ser
 100 105 110

gat ttt gaa tac tac aac cgg gag ctg aga ccc cat aat atc gat gag 384
 Asp Phe Glu Tyr Tyr Asn Arg Glu Leu Arg Pro His Asn Ile Asp Glu
 115 120 125

gag gtg ttg ggt tgg cag aga ctg tgc tac gtg ata gaa tcg ggt cta 432

Tyr Val Ala Glu Pro Phe Leu Pro Phe Thr Leu Gly Thr Tyr Met Leu
370 375 380

Val Leu Lys Asn Cys Tyr Arg Leu Leu Ala Leu Met Gln Glu Ser Met
385 390 395 400

<210> 27

<211> 1140

<212> DNA

<213> *Drosophila melanogaster*

<220>

<221> CDS

<222> (1)..(1137)

<223> DOR 59D.1, a coding region on BDGP Clone No.
AC005672

<400> 27

atg gca gag gtc aga gtg gac agt ctg gag ttt ttc aag agc cat tgg 48
Met Ala Glu Val Arg Val Asp Ser Leu Glu Phe Phe Lys Ser His Trp
1 5 10 15

acc gcc tgg cgg tac ttg gga gtg gct cat ttt cgg gtc gag aac tgg 96
Thr Ala Trp Arg Tyr Leu Gly Val Ala His Phe Arg Val Glu Asn Trp
20 25 30

aag aac ctt tac gtg ttt tac agc att gtg tcg aat ctt ctc gtg acc 144
Lys Asn Leu Tyr Val Phe Tyr Ser Ile Val Ser Asn Leu Leu Val Thr
35 40 45

ctg tgc tac ccc gtt cac ctg gga ata tcc ctc ttt cgc aac cgc acc 192
Leu Cys Tyr Pro Val His Leu Gly Ile Ser Leu Phe Arg Asn Arg Thr
50 55 60

atc acc gag gac atc ctc aac ctg acc acc ttt gcg acc tgc aca gcc 240
Ile Thr Glu Asp Ile Leu Asn Leu Thr Thr Phe Ala Thr Cys Thr Ala
65 70 75 80

tgt tcg gtg aag tgc ctg ctc tac gcc tac aac atc aag gat gtg ctg 288
Cys Ser Val Lys Cys Leu Leu Tyr Ala Tyr Asn Ile Lys Asp Val Leu
85 90 95

gag atg gag cgg ctg ttg agg ctt ttg gat gaa cgc gtc gtg ggt ccg 336
Glu Met Glu Arg Leu Leu Arg Leu Leu Asp Glu Arg Val Val Gly Pro
100 105 110

acc gac aac gag tac tgg ttc gga cgc ctc cac tac gcg gcc ttc agt 960
 Thr Asp Asn Glu Tyr Trp Phe Gly Arg Leu His Tyr Ala Ala Phe Ser
 305 310 315 320

tgc aat tgg cac aca cag aac agg agc ttt aag cgg aaa atg atg ctg 1008
 Cys Asn Trp His Thr Gln Asn Arg Ser Phe Lys Arg Lys Met Met Leu
 325 330 335

ttc gtt gag caa tgc ttg aag aag agc acc gct gtg gct gcc gga atg 1056
 Phe Val Glu Gln Ser Leu Lys Lys Ser Thr Ala Val Ala Gly Gly Met
 340 345 350

atg cgt atc cac ctg gac acg ttc ttt tcc acc cta aag ggg gcc tac 1104
 Met Arg Ile His Leu Asp Thr Phe Phe Ser Thr Leu Lys Gly Ala Tyr
 355 360 365

tcc ctc ttt acc atc att att cgg atg aga aag tag 1140
 Ser Leu Phe Thr Ile Ile Ile Arg Met Arg Lys
 370 375

<210> 28
 <211> 379
 <212> PRT
 <213> Drosophila melanogaster

<400> 28
 Met Ala Glu Val Arg Val Asp Ser Leu Glu Phe Phe Lys Ser His Trp
 1 5 10 15

Thr Ala Trp Arg Tyr Leu Gly Val Ala His Phe Arg Val Glu Asn Trp
 20 25 30

Lys Asn Leu Tyr Val Phe Tyr Ser Ile Val Ser Asn Leu Leu Val Thr
 35 40 45

Leu Cys Tyr Pro Val His Leu Gly Ile Ser Leu Phe Arg Asn Arg Thr
 50 55 60

Ile Thr Glu Asp Ile Leu Asn Leu Thr Thr Phe Ala Thr Cys Thr Ala
 65 70 75 80

Cys Ser Val Lys Cys Leu Leu Tyr Ala Tyr Asn Ile Lys Asp Val Leu
 85 90 95

Glu Met Glu Arg Leu Leu Arg Leu Leu Asp Glu Arg Val Val Gly Pro
 100 105 110

Ser Leu Phe Thr Ile Ile Ile Arg Met Arg Lys
 370 375

<210> 29
 <211> 1194
 <212> DNA
 <213> Drosophila melanogaster

<220>
 <221> CDS
 <222> (1)..(1194)
 <223> DOR 2F.1, coding region of NCBI Accession No.
 AL009195

<400> 29
 atg gag aag caa gag gat ttc aaa ctg aac acc cac agt gct gtg tac 48
 Met Glu Lys Gln Glu Asp Phe Lys Leu Asn Thr His Ser Ala Val Tyr
 1 5 10 15
 tac cac tgg cgc gtt tgg gag ctc act ggc ctg atg cgt cct ccg ggc 96
 Tyr His Trp Arg Val Trp Glu Leu Thr Gly Leu Met Arg Pro Pro Gly
 20 25 30
 gtt tca agc ctg ott tac gtg gta tac tcc att acg gtc aac ttg gtg 144
 Val Ser Ser Leu Leu Tyr Val Val Tyr Ser Ile Thr Val Asn Leu Val
 35 40 45
 gtc acc gtg ctg ttt ccc ttg agc ttg ctg gcc agg ctg ctg ttc acc 192
 Val Thr Val Leu Phe Pro Leu Ser Leu Leu Ala Arg Leu Leu Phe Thr
 50 55 60
 acc aac atg gcc gga ttg tgc gag aac ctg acc ata act att acc gat 240
 Thr Asn Met Ala Gly Leu Cys Glu Asn Leu Thr Ile Thr Ile Thr Asp
 65 70 75 80
 att gtg gcc aat ttg aag ttt gcg aat gtg tac atg gtg agg aag cag 288
 Ile Val Ala Asn Leu Lys Phe Ala Asn Val Tyr Met Val Arg Lys Gln
 85 90 95
 ctc cat gag att cgc tct ctc cta agg ctc atg gac gct aga gcc cgg 336
 Leu His Glu Ile Arg Ser Leu Leu Arg Leu Met Asp Ala Arg Ala Arg
 100 105 110
 ctg gtg ggc gat ccc gag gag att tct gcc ttg agg aag gaa gtg aat 384
 Leu Val Gly Asp Pro Glu Glu Ile Ser Ala Leu Arg Lys Glu Val Asn

[illegible]

Thr Ser Ala Asp Arg Arg Tyr Lys Ser Thr Leu Val Tyr Phe Leu His
 340 345 350

Asn Leu Gln Gln Pro Ile Thr Leu Thr Ala Gly Gly Val Phe Pro Ile
 355 360 365

Ser Met Gln Thr Asn Leu Ala Met Val Lys Leu Ala Phe Ser Val Val
 370 375 380

Thr Val Ile Lys Gln Phe Asn Leu Ala Glu Arg Phe Gln
 385 390 395

<210> 33

<211> 1200

<212> DNA

<213> Drosophila melanogaster

<220>

<221> CDS

<222> (1)..(1200)

<223> DOR 36E.1

<400> 33

atg gtt cgt tac gtg ccc cgg ttc gct gat ggt cag aaa gta aag ttg 48
 Met Val Arg Tyr Val Pro Arg Phe Ala Asp Gly Gln Lys Val Lys Leu
 1 5 10 15

gct tgg ccc ttg gcg gtt ttt cgg tta aat cac ata ttc tgg cca ttg 96
 Ala Trp Pro Leu Ala Val Phe Arg Leu Asn His Ile Phe Trp Pro Leu
 20 25 30

gat ccg agc aca ggg aaa tgg ggc cga tat ctg gac aag gtt cta gct 144
 Asp Pro Ser Thr Gly Lys Trp Gly Arg Tyr Leu Asp Lys Val Leu Ala
 35 40 45

gtt gcg atg tcc ttg gtt ttt atg caa cac aac gat gca gag ctg agg 192
 Val Ala Met Ser Leu Val Phe Met Gln His Asn Asp Ala Glu Leu Arg
 50 55 60

tac ttg cgc ttc gag gca agt aat cgg aat ttg gat gcc ttt ctc aca 240
 Tyr Leu Arg Phe Glu Ala Ser Asn Arg Asn Leu Asp Ala Phe Leu Thr
 65 70 75 80

gga atg cca acg tat tta atc ctc gtg gag gct caa ttt aga agt ctt 288
 Gly Met Pro Thr Tyr Leu Ile Leu Val Glu Ala Gln Phe Arg Ser Leu
 85 90 95

cac att cta ctg cac ttc gag aag ctt cag aag ttt tta gaa ata ttc	336
His Ile Leu Leu His Phe Glu Lys Leu Gln Lys Phe Leu Glu Ile Phe	
100 105 110	
tac gca aat att tat att gat ccc cgt aag gaa ccc gaa atg ttt cga	384
Tyr Ala Asn Ile Tyr Ile Asp Pro Arg Lys Glu Pro Glu Met Phe Arg	
115 120 125	
aaa gtg gat gga aag atg ata att aac aga tta gtt tcg gcc atg tac	432
Lys Val Asp Gly Lys Met Ile Ile Asn Arg Leu Val Ser Ala Met Tyr	
130 135 140	
ggt gca gtt atc tct ctg tat cta atc gca ccc gtt ttt tcc atc att	480
Gly Ala Val Ile Ser Leu Tyr Leu Ile Ala Pro Val Phe Ser Ile Ile	
145 150 155 160	
aac caa agc aaa gat ttt cta tac tct atg atc ttt ccg ttc gat tcg	528
Asn Gln Ser Lys Asp Phe Leu Tyr Ser Met Ile Phe Pro Phe Asp Ser	
165 170 175	
gat ccc ttg tac ata ttt gtg cca ctg ctt ttg aca aac gta tgg gtt	576
Asp Pro Leu Tyr Ile Phe Val Pro Leu Leu Leu Thr Asn Val Trp Val	
180 185 190	
ggc att gta ata gat acc atg atg ttc ggg gag acg aat ttg ttg tgt	624
Gly Ile Val Ile Asp Thr Met Met Phe Gly Glu Thr Asn Leu Leu Cys	
195 200 205	
gaa cta att gtc cac cta aat ggt agt tat atg ttg ctc aag agg gac	672
Glu Leu Ile Val His Leu Asn Gly Ser Tyr Met Leu Leu Lys Arg Asp	
210 215 220	
ttg cag ttg gcc att gaa aag ata tta gtt gca agg gac cgt ccg cat	720
Leu Gln Leu Ala Ile Glu Lys Ile Leu Val Ala Arg Asp Arg Pro His	
225 230 235 240	
atg gcc aaa cag cta aag gtt tta att aca aaa act ctc cga aag aat	768
Met Ala Lys Gln Leu Lys Val Leu Ile Thr Lys Thr Leu Arg Lys Asn	
245 250 255	
gtg gct cta aat cag ttt ggc cag cag ctg gag gct cag tat act gtg	816
Val Ala Leu Asn Gln Phe Gly Gln Gln Leu Glu Ala Gln Tyr Thr Val	
260 265 270	
cgg gtt ttt att atg ttt gca ttc gct gcg ggc ctt tta tgt gct ctt	864
Arg Val Phe Ile Met Phe Ala Phe Ala Ala Gly Leu Leu Cys Ala Leu	
275 280 285	

tct ttt aag gct tat acg acg gat tcc ctc agc aca atg tac tac ctt	912
Ser Phe Lys Ala Tyr Thr Thr Asp Ser Leu Ser Thr Met Tyr Tyr Leu	
290 295 300	
acc cat tgg gag caa atc ctg cag tac tct aca aat ccc agc gaa aat	960
Thr His Trp Glu Gln Ile Leu Gln Tyr Ser Thr Asn Pro Ser Glu Asn	
305 310 315 320	
ctg cga tta cta aag ctc att aac ttg gcc att gag atg aac agc aag	1008
Leu Arg Leu Leu Lys Leu Ile Asn Leu Ala Ile Glu Met Asn Ser Lys	
325 330 335	
ccc ttc tat gtg aca ggg cta aaa tat ttt cgc gtt agt ctg cag gct	1056
Pro Phe Tyr Val Thr Gly Leu Lys Tyr Phe Arg Val Ser Leu Gln Ala	
340 345 350	
ggc tta aaa gta agt gaa aaa cga gtg caa aac cat ttc act gtc agc	1104
Gly Leu Lys Val Ser Glu Lys Arg Val Gln Asn His Phe Thr Val Ser	
355 360 365	
tct ttc aca gat tct gca ggc atc ctt ctc gta ctt cac att cct cac	1152
Ser Phe Thr Asp Ser Ala Gly Ile Leu Leu Val Leu His Ile Pro His	
370 375 380	
ttc gat gca gcg acg aca aat gag caa tta aat aat tca cat ttt ttt	1200
Phe Asp Ala Ala Thr Thr Asn Glu Gln Leu Asn Asn Ser His Phe Phe	
385 390 395 400	

<210> 34
 <211> 400
 <212> PRT
 <213> Drosophila melanogaster

<400> 34
 Met Val Arg Tyr Val Pro Arg Phe Ala Asp Gly Gln Lys Val Lys Leu
 1 5 10 15
 Ala Trp Pro Leu Ala Val Phe Arg Leu Asn His Ile Phe Trp Pro Leu
 20 25 30
 Asp Pro Ser Thr Gly Lys Trp Gly Arg Tyr Leu Asp Lys Val Leu Ala
 35 40 45
 Val Ala Met Ser Leu Val Phe Met Gln His Asn Asp Ala Glu Leu Arg
 50 55 60

Tyr Leu Arg Phe Glu Ala Ser Asn Arg Asn Leu Asp Ala Phe Leu Thr
65 70 75 80

Gly Met Pro Thr Tyr Leu Ile Leu Val Glu Ala Gln Phe Arg Ser Leu
85 90 95

His Ile Leu Leu His Phe Glu Lys Leu Gln Lys Phe Leu Glu Ile Phe
100 105 110

Tyr Ala Asn Ile Tyr Ile Asp Pro Arg Lys Glu Pro Glu Met Phe Arg
115 120 125

Lys Val Asp Gly Lys Met Ile Ile Asn Arg Leu Val Ser Ala Met Tyr
130 135 140

Gly Ala Val Ile Ser Leu Tyr Leu Ile Ala Pro Val Phe Ser Ile Ile
145 150 155 160

Asn Gln Ser Lys Asp Phe Leu Tyr Ser Met Ile Phe Pro Phe Asp Ser
165 170 175

Asp Pro Leu Tyr Ile Phe Val Pro Leu Leu Leu Thr Asn Val Trp Val
180 185 190

Gly Ile Val Ile Asp Thr Met Met Phe Gly Glu Thr Asn Leu Leu Cys
195 200 205

Glu Leu Ile Val His Leu Asn Gly Ser Tyr Met Leu Leu Lys Arg Asp
210 215 220

Leu Gln Leu Ala Ile Glu Lys Ile Leu Val Ala Arg Asp Arg Pro His
225 230 235 240

Met Ala Lys Gln Leu Lys Val Leu Ile Thr Lys Thr Leu Arg Lys Asn
245 250 255

Val Ala Leu Asn Gln Phe Gly Gln Gln Leu Glu Ala Gln Tyr Thr Val
260 265 270

Arg Val Phe Ile Met Phe Ala Phe Ala Ala Gly Leu Leu Cys Ala Leu
275 280 285

Ser Phe Lys Ala Tyr Thr Thr Asp Ser Leu Ser Thr Met Tyr Tyr Leu
290 295 300

Thr His Trp Glu Gln Ile Leu Gln Tyr Ser Thr Asn Pro Ser Glu Asn
305 310 315 320

ttt ctg ctg atc ggc ctg gtt ctg ggc ttc acg ctg atc aac gtg ttt 864
Phe Leu Leu Ile Gly Leu Val Leu Gly Phe Thr Leu Ile Asn Val Phe
275 280 285

ttc ttc tca gac atc tgg acg ggc atc gca tca ttt atg ttt gtt ata 912
Phe Phe Ser Asp Ile Trp Thr Gly Ile Ala Ser Phe Met Phe Val Ile
290 295 300

acc att ttg ctg cag acc ttc ccc ttc tgc tac aca tgc aac ctc atc 960
Thr Ile Leu Leu Gln Thr Phe Pro Phe Cys Tyr Thr Cys Asn Leu Ile
305 310 315 320

atg gag gac tgc gag tcc ttg acc cat gct att ttc cag tcc aac tgg 1008
Met Glu Asp Cys Glu Ser Leu Thr His Ala Ile Phe Gln Ser Asn Trp
325 330 335

gtg gat gcc agt cgt cgc tac aaa aca aca cta ctg tat ttt ctc caa 1056
Val Asp Ala Ser Arg Arg Tyr Lys Thr Thr Leu Leu Tyr Phe Leu Gln
340 345 350

aac gtg cag cag cct atc gtt ttc att gca ggc ggt atc ttt cag ata 1104
Asn Val Gln Gln Pro Ile Val Phe Ile Ala Gly Gly Ile Phe Gln Ile
355 360 365

tcc atg agc agc aac ata agt gtg gca aag ttt gct ttc tcc gtg ata 1152
Ser Met Ser Ser Asn Ile Ser Val Ala Lys Phe Ala Phe Ser Val Ile
370 375 380

acc att acc aag caa atg aat ata gct gac aaa ttt aag acg gac 1197
Thr Ile Thr Lys Gln Met Asn Ile Ala Asp Lys Phe Lys Thr Asp
385 390 395

<210> 36

<211> 399

<212> PRT

<213> Drosophila melanogaster

<400> 36

Met Val Phe Glu Leu Ile Arg Pro Ala Pro Leu Thr Glu Gln Lys Arg
1 5 10 15

Ser Arg Asp Gly Cys Ile Tyr Leu Tyr Arg Ala Met Lys Phe Ile Gly
20 25 30

Trp Leu Pro Pro Lys Gln Gly Val Leu Arg Tyr Val Tyr Leu Thr Trp
35 40 45

Thr Ile Leu Leu Gln Thr Phe Pro Phe Cys Tyr Thr Cys Asn Leu Ile
305 310 315 320

Met Glu Asp Cys Glu Ser Leu Thr His Ala Ile Phe Gln Ser Asn Trp
325 330 335

Val Asp Ala Ser Arg Arg Tyr Lys Thr Thr Leu Leu Tyr Phe Leu Gln
340 345 350

Asn Val Gln Gln Pro Ile Val Phe Ile Ala Gly Gly Ile Phe Gln Ile
355 360 365

Ser Met Ser Ser Asn Ile Ser Val Ala Lys Phe Ala Phe Ser Val Ile
370 375 380

Thr Ile Thr Lys Gln Met Asn Ile Ala Asp Lys Phe Lys Thr Asp
385 390 395

<210> 37
<211> 1218
<212> DNA
<213> Drosophila melanogaster

<220>
<221> CDS
<222> (1)..(1218)
<223> DOR 41E.2

<400> 37
atg gat ctg cga agg tgg ttt ccg acc ttg tac acc cag tcg aag gat 48
Met Asp Leu Arg Arg Trp Phe Pro Thr Leu Tyr Thr Gln Ser Lys Asp
1 5 10 15

tcg cca gtt cgc tcc cga gac gcg acc ctg tac ctc cta cgc tgc gtc 96
Ser Pro Val Arg Ser Arg Asp Ala Thr Leu Tyr Leu Leu Arg Cys Val
20 25 30

ttc tta atg ggc gtc cgc aag cca cct gcc aag ttt ttc gtg gcc tac 144
Phe Leu Met Gly Val Arg Lys Pro Pro Ala Lys Phe Phe Val Ala Tyr
35 40 45

gtg ctc tgg tcc ttc gca ctg aat ttc tgc tca aca ttt tat cag cca 192
Val Leu Trp Ser Phe Ala Leu Asn Phe Cys Ser Thr Phe Tyr Gln Pro
50 55 60

att ggc ttt ctc aca ggc tat ata agc cat tta tca gag ttc tcc ccg 240

Ser Pro Val Arg Ser Arg Asp Ala Thr Leu Tyr Leu Leu Arg Cys Val
 20 25 30

Phe Leu Met Gly Val Arg Lys Pro Pro Ala Lys Phe Phe Val Ala Tyr
 35 40 45

Val Leu Trp Ser Phe Ala Leu Asn Phe Cys Ser Thr Phe Tyr Gln Pro
 50 55 60

Ile Gly Phe Leu Thr Gly Tyr Ile Ser His Leu Ser Glu Phe Ser Pro
 65 70 75 80

Gly Glu Phe Leu Thr Ser Leu Gln Val Ala Phe Asn Ala Trp Ser Cys
 85 90 95

Ser Thr Lys Val Leu Ile Val Trp Ala Leu Val Lys Arg Phe Asp Glu
 100 105 110

Ala Asn Asn Leu Leu Asp Glu Met Asp Arg Arg Ile Thr Asp Pro Gly
 115 120 125

Glu Arg Leu Gln Ile His Arg Ala Val Ser Leu Ser Asn Arg Ile Phe
 130 135 140

Phe Phe Phe Met Ala Val Tyr Met Val Tyr Ala Thr Asn Thr Phe Leu
 145 150 155 160

Ser Ala Ile Phe Ile Gly Arg Pro Pro Tyr Gln Asn Tyr Tyr Pro Phe
 165 170 175

Leu Asp Trp Arg Ser Ser Thr Leu His Leu Ala Leu Gln Ala Gly Leu
 180 185 190

Glu Tyr Phe Ala Met Ala Gly Ala Cys Phe Gln Asp Val Cys Val Asp
 195 200 205

Cys Tyr Pro Val Asn Phe Val Leu Val Leu Arg Ala His Met Ser Ile
 210 215 220

Phe Ala Glu Arg Leu Arg Arg Leu Gly Thr Tyr Pro Tyr Glu Ser Gln
 225 230 235 240

Glu Gln Lys Tyr Glu Arg Leu Val Gln Cys Ile Gln Asp His Lys Val
 245 250 255

Ile Leu Arg Phe Val Asp Cys Leu Arg Pro Val Ile Ser Gly Thr Ile
 260 265 270

009240 451600

Phe Val Gln Phe Leu Val Val Gly Leu Val Leu Gly Phe Thr Leu Ile
275 280 285

Asn Ile Val Leu Phe Ala Asn Leu Gly Ser Ala Ile Ala Ala Leu Ser
290 295 300

Phe Met Ala Ala Val Leu Leu Glu Thr Thr Pro Phe Cys Ile Leu Cys
305 310 315 320

Asn Tyr Leu Thr Glu Asp Cys Tyr Lys Leu Ala Asp Ala Leu Phe Gln
325 330 335

Ser Asn Trp Ile Asp Glu Glu Lys Arg Tyr Gln Lys Thr Leu Met Tyr
340 345 350

Phe Leu Gln Lys Leu Gln Gln Pro Ile Thr Phe Met Ala Met Asn Val
355 360 365

Phe Pro Ile Ser Val Gly Thr Asn Ile Ser Val Thr Lys Phe Ser Phe
370 375 380

Ser Val Phe Thr Leu Val Lys Gln Met Asn Ile Ser Glu Lys Leu Ala
385 390 395 400

Lys Ser Glu Met Glu Glu
405

<210> 39
<211> 1188
<212> DNA
<213> Drosophila melanogaster

<220>
<221> CDS
<222> (1)..(1188)
<223> DOR 45F.1

<400> 39
atg tat ccg cga ttc ctc agc cgt aac tat ccg ctg gcc aag cat ttg 48
Met Tyr Pro Arg Phe Leu Ser Arg Asn Tyr Pro Leu Ala Lys His Leu
1 5 10 15

ttc ttc gtc acc aga tac tcc ttt ggc ctg ctg ggc ctg aga ttt ggc 96
Phe Phe Val Thr Arg Tyr Ser Phe Gly Leu Leu Gly Leu Arg Phe Gly
20 25 30

aaa gag caa tgc tgg ctt cac ctc ttg tgg ctg gtg ttc aat ttc gtt	144
Lys Glu Gln Ser Trp Leu His Leu Leu Trp Leu Val Phe Asn Phe Val	
35 40 45	
aac ctg gcg cac tgc tgc cag gcg gag ttc gtc ttc ggc tgg agt cac	192
Asn Leu Ala His Cys Cys Gln Ala Glu Phe Val Phe Gly Trp Ser His	
50 55 60	
ttg cgc acc agt ccc gtg gat gcc atg gac gcc ttt tgt cct ctg gcc	240
Leu Arg Thr Ser Pro Val Asp Ala Met Asp Ala Phe Cys Pro Leu Ala	
65 70 75 80	
tgc agt ttc acc acg ctc ttc aag ctg gga tgg atg tgg tgg cgt cgc	288
Cys Ser Phe Thr Thr Leu Phe Lys Leu Gly Trp Met Trp Trp Arg Arg	
85 90 95	
cag gaa gta gct gat cta atg gac cgc atc cgc ttg ctc atc ggg gag	336
Gln Glu Val Ala Asp Leu Met Asp Arg Ile Arg Leu Leu Ile Gly Glu	
100 105 110	
cag gag aag agg gag gac tcc cgg aga aag gtg gct caa agg agc tac	384
Gln Glu Lys Arg Glu Asp Ser Arg Arg Lys Val Ala Gln Arg Ser Tyr	
115 120 125	
tat ctc atg gtc acc agg tgc ggt atg ctg gtc ttc acc ctg ggc agc	432
Tyr Leu Met Val Thr Arg Cys Gly Met Leu Val Phe Thr Leu Gly Ser	
130 135 140	
att acc act gga gcc ttc gtt ctg cgt tcc ctt tgg gaa atg tgg gtg	480
Ile Thr Thr Gly Ala Phe Val Leu Arg Ser Leu Trp Glu Met Trp Val	
145 150 155 160	
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Arg Arg His Gln Glu Phe Lys Phe Asp Met Pro Phe Arg Met Leu Phe	
165 170 175	
cac gac ttt gcg cat cgc atg ccc tgg ttt cca gtt ttc tat ctc tac	576
His Asp Phe Ala His Arg Met Pro Trp Phe Pro Val Phe Tyr Leu Tyr	
180 185 190	
tcc aca tgg agt ggc cag gtc act gtg tac gcc ttt gct ggt aca gat	624
Ser Thr Trp Ser Gly Gln Val Thr Val Tyr Ala Phe Ala Gly Thr Asp	
195 200 205	
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Gly Phe Phe Phe Gly Phe Thr Leu Tyr Met Ala Phe Leu Leu Gln Ala	
210 215 220	

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Leu Arg Tyr Asp Ile Gln Asp Ala Leu Lys Pro Ile Arg Asp Pro Ser	
225 230 235 240	
ctt agg gaa tcc aaa atc tgc tgt cag cga ttg gcg gac atc gtg gat	768
Leu Arg Glu Ser Lys Ile Cys Cys Gln Arg Leu Ala Asp Ile Val Asp	
245 250 255	
cgc cac aat gag ata gag aag ata gtc aag gaa ttt tct gga att atg	816
Arg His Asn Glu Ile Glu Lys Ile Val Lys Glu Phe Ser Gly Ile Met	
260 265 270	
gct gct cca act ttt gtt cac ttc gta tca gcc agc tta gtg ata gcc	864
Ala Ala Pro Thr Phe Val His Phe Val Ser Ala Ser Leu Val Ile Ala	
275 280 285	
acc agc gtc att gat ata cta ttg tat tcc ggc tat aac atc atc cgt	912
Thr Ser Val Ile Asp Ile Leu Leu Tyr Ser Gly Tyr Asn Ile Ile Arg	
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Tyr Val Val Tyr Thr Phe Thr Val Ser Ser Ala Ile Phe Leu Tyr Cys	
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Tyr Gly Gly Thr Glu Met Ser Thr Glu Ser Leu Ser Leu Gly Glu Ala	
325 330 335	
gcc tac agc agt gcc tgg tat act tgg gat cga gag acc cgc agg cgg	1056
Ala Tyr Ser Ser Ala Trp Tyr Thr Trp Asp Arg Glu Thr Arg Arg Arg	
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Val Phe Leu Ile Ile Leu Arg Ala Gln Arg Pro Ile Thr Val Arg Val	
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ccc ttt ttt gca cca tcg tta cca gtc ttc aca tcg gtc atc aag ttt	1152
Pro Phe Phe Ala Pro Ser Leu Pro Val Phe Thr Ser Val Ile Lys Phe	
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Arg His Asn Glu Ile Glu Lys Ile Val Lys Glu Phe Ser Gly Ile Met
 260 265 270

Ala Ala Pro Thr Phe Val His Phe Val Ser Ala Ser Leu Val Ile Ala
 275 280 285

Thr Ser Val Ile Asp Ile Leu Leu Tyr Ser Gly Tyr Asn Ile Ile Arg
 290 295 300

Tyr Val Val Tyr Thr Phe Thr Val Ser Ser Ala Ile Phe Leu Tyr Cys
 305 310 315 320

Tyr Gly Gly Thr Glu Met Ser Thr Glu Ser Leu Ser Leu Gly Glu Ala
 325 330 335

Ala Tyr Ser Ser Ala Trp Tyr Thr Trp Asp Arg Glu Thr Arg Arg Arg
 340 345 350

Val Phe Leu Ile Ile Leu Arg Ala Gln Arg Pro Ile Thr Val Arg Val
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Phe Trp Ala Leu Leu Tyr Asp Lys Asn Leu Arg Arg Tyr Val Cys Ile	
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gga ctg gcc tca ttc cac atc ttc acc caa atc gtc tac atg atg agt	144
Gly Leu Ala Ser Phe His Ile Phe Thr Gln Ile Val Tyr Met Met Ser	
35 40 45	
acc aat gaa gga cta acc ggg ata att cgt aac tca tat atg ctc gtc	192
Thr Asn Glu Gly Leu Thr Gly Ile Ile Arg Asn Ser Tyr Met Leu Val	
50 55 60	
ctt tgg att aat acg gtg ctg cga gct tat ctc ttg ctg gcg gat cac	240
Leu Trp Ile Asn Thr Val Leu Arg Ala Tyr Leu Leu Leu Ala Asp His	
65 70 75 80	
gac aga tat ttg gct ttg atc caa aaa cta act gag gcc tat tac gat	288
Asp Arg Tyr Leu Ala Leu Ile Gln Lys Leu Thr Glu Ala Tyr Tyr Asp	
85 90 95	
tta ctg aat ctg aac gat tcg tat ata tcg gaa ata ttg gac cag gtg	336
Leu Leu Asn Leu Asn Asp Ser Tyr Ile Ser Glu Ile Leu Asp Gln Val	
100 105 110	
aac aag gtg gga aag ttg atg gct agg ggc aat ctg ttc ttt ggc atg	384
Asn Lys Val Gly Lys Leu Met Ala Arg Gly Asn Leu Phe Phe Gly Met	
115 120 125	
ctc aca tcc atg gga ttc ggt ctg tac cca ttg tcc tcc agc gaa aga	432
Leu Thr Ser Met Gly Phe Gly Leu Tyr Pro Leu Ser Ser Ser Glu Arg	
130 135 140	
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Ala Leu Asn Phe Lys Thr His Phe Pro Phe Ala Val Leu Pro Phe Gly	
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Ser Lys Ile Pro Gly Leu Asn Glu Tyr Glu Ser Pro Tyr Tyr Glu Met	
165 170 175	
tgg tac atc ttt cag atg ctc atc acc ccg atg ggc tgt tgc atg tac	576
Trp Tyr Ile Phe Gln Met Leu Ile Thr Pro Met Gly Cys Cys Met Tyr	
180 185 190	
att ccg tac acc agt ctg att gtg ggc ttg ata atg ttc ggc att gtg	624
Ile Pro Tyr Thr Ser Leu Ile Val Gly Leu Ile Met Phe Gly Ile Val	
195 200 205	

Met Phe Glu Asp Ile Gln Leu Ile Tyr Met Asn Ile Lys Ile Leu Arg
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Gly Leu Ala Ser Phe His Ile Phe Thr Gln Ile Val Tyr Met Met Ser
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50 55 60

Leu Trp Ile Asn Thr Val Leu Arg Ala Tyr Leu Leu Leu Ala Asp His
65 70 75 80

Asp Arg Tyr Leu Ala Leu Ile Gln Lys Leu Thr Glu Ala Tyr Tyr Asp
85 90 95

Leu Leu Asn Leu Asn Asp Ser Tyr Ile Ser Glu Ile Leu Asp Gln Val
100 105 110

Asn Lys Val Gly Lys Leu Met Ala Arg Gly Asn Leu Phe Phe Gly Met
115 120 125

Leu Thr Ser Met Gly Phe Gly Leu Tyr Pro Leu Ser Ser Ser Glu Arg
130 135 140

Ala Leu Asn Phe Lys Thr His Phe Pro Phe Ala Val Leu Pro Phe Gly
145 150 155 160

Ser Lys Ile Pro Gly Leu Asn Glu Tyr Glu Ser Pro Tyr Tyr Glu Met
165 170 175

Trp Tyr Ile Phe Gln Met Leu Ile Thr Pro Met Gly Cys Cys Met Tyr
180 185 190

Ile Pro Tyr Thr Ser Leu Ile Val Gly Leu Ile Met Phe Gly Ile Val
195 200 205

Arg Cys Lys Ala Leu Gln His Arg Leu Arg Gln Val Ala Leu Lys His
210 215 220

Pro Tyr Gly Asp Arg Asp Pro Arg Glu Leu Arg Glu Glu Ile Ile Ala
225 230 235 240

Cys Ile Arg Tyr Gln Gln Ser Ile Ile Glu Tyr Met Asp His Ile Asn
245 250 255

Glu Leu Thr Thr Met Met Phe Leu Phe Glu Leu Met Ala Phe Ser Ala
260 265 270

Leu Leu Cys Ala Leu Leu Phe Met Leu Ile Ile Val Ser Gly Thr Ser
275 280 285

Gln Leu Ile Ile Val Cys Met Tyr Ile Asn Met Ile Leu Ala Gln Ile
290 295 300

Leu Ala Leu Tyr Trp Tyr Ala Asn Glu Leu Arg Glu Gln Asn Leu Ala
305 310 315 320

Val Ala Thr Ala Ala Tyr Glu Thr Glu Trp Phe Thr Phe Asp Val Pro
325 330 335

Leu Arg Lys Asn Ile Leu Phe Met Met Met Arg Ala Gln Arg Pro Ala
340 345 350

Ala Ile Leu Leu Gly Asn Ile Arg Pro Ile Thr Leu Glu Leu Phe Gln
355 360 365

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Tyr Gly
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Leu	Ser	Pro	Thr	Thr	Phe	Glu	Asp	Pro	Ile	Phe	Gly	Thr	His	Leu	Arg	
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Tyr	Phe	Gln	Trp	Tyr	Gly	Tyr	Val	Ala	Ser	Lys	Asp	Gln	Asn	Arg	Pro	
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Leu	Leu	Ser	Leu	Ile	Arg	Cys	Thr	Ile	Leu	Thr	Ala	Ser	Ile	Trp	Leu	
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Ser	Cys	Ala	Leu	Met	Leu	Ala	Arg	Val	Phe	Arg	Gly	Tyr	Glu	Asn	Leu	
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aat	gat	ggg	gcc	aca	agt	tac	gcc	acc	gca	gtc	cag	tat	ttc	gcg	gta	288
Asn	Asp	Gly	Ala	Thr	Ser	Tyr	Ala	Thr	Ala	Val	Gln	Tyr	Phe	Ala	Val	
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tcg	att	gcc	atg	ttt	aat	gct	tac	gta	caa	aga	gat	aga	tat	gtt	ctt	336
Ser	Ile	Ala	Met	Phe	Asn	Ala	Tyr	Val	Gln	Arg	Asp	Arg	Tyr	Val	Leu	
			100					105					110			
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Leu	Tyr	Leu	His	Ile	Val	Leu	Glu	Val	Ile	Ser	Leu	Leu	Arg	Val	Ala	
		115					120					125				
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His	Ser	Asp	Ile	Gln	Asn	Leu	Met	His	Glu	Ala	Asp	Asn	Arg	Glu	Met	
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gaa	ctt	ttg	gtc	gcc	act	cag	gct	tat	aca	cga	acc	att	acc	ctg	ttg	480
Glu	Leu	Leu	Val	Ala	Thr	Gln	Ala	Tyr	Thr	Arg	Thr	Ile	Thr	Leu	Leu	
145					150					155				160		
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Ile	Trp	Ile	Pro	Ser	Val	Ile	Ala	Gly	Leu	Met	Ala	Tyr	Ser	Asp	Cys	
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atc	tac	agg	agt	ctg	ttt	ctg	ccg	aaa	tcg	gtt	ttc	aat	gtg	cca	gct	576
Ile	Tyr	Arg	Ser	Leu	Phe	Leu	Pro	Lys	Ser	Val	Phe	Asn	Val	Pro	Ala	
			180					185				190				
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Val	Arg	Arg	Gly	Glu	Glu	His	Pro	Ile	Leu	Leu	Phe	Gln	Leu	Phe	Pro		
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Phe	Gly	Glu	Leu	Cys	Asp	Asn	Phe	Val	Val	Gly	Tyr	Leu	Gly	Pro	Trp		
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Tyr	Ala	Leu	Gly	Leu	Gly	Ile	Thr	Ala	Ile	Pro	Leu	Trp	His	Thr	Phe		
	225				230					235					240		
atc	act	tgc	ctc	atg	aag	tac	gta	aat	ctc	aag	ctg	caa	ata	ctc	aac	768	
Ile	Thr	Cys	Leu	Met	Lys	Tyr	Val	Asn	Leu	Lys	Leu	Gln	Ile	Leu	Asn		
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Lys	Arg	Val	Glu	Glu	Met	Asp	Ile	Thr	Arg	Leu	Asn	Ser	Lys	Leu	Val		
		260						265					270				
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Ile	Gly	Arg	Leu	Thr	Ala	Ser	Glu	Leu	Thr	Phe	Trp	Gln	Met	Gln	Leu		
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Phe	Lys	Glu	Phe	Val	Lys	Glu	Gln	Leu	Arg	Ile	Arg	Lys	Phe	Val	Gln		
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Glu	Leu	Gln	Tyr	Leu	Ile	Cys	Val	Pro	Val	Met	Ala	Asp	Phe	Ile	Ile		
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Phe	Ser	Val	Leu	Ile	Cys	Phe	Leu	Phe	Phe	Ala	Leu	Thr	Val	Gly	Val		
			325					330					335				
cca	agc	aaa	atg	gat	tac	ttc	ttc	atg	ttc	att	tac	ctt	ttt	gtg	atg	1056	
Pro	Ser	Lys	Met	Asp	Tyr	Phe	Phe	Met	Phe	Ile	Tyr	Leu	Phe	Val	Met		
		340						345				350					
gct	ggt	ata	ttg	tgg	att	tat	cat	tgg	cat	gcc	acg	ttg	att	gtt	gaa	1104	
Ala	Gly	Ile	Leu	Trp	Ile	Tyr	His	Trp	His	Ala	Thr	Leu	Ile	Val	Glu		
	355					360				365							
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Cys	His	Asp	Glu	Leu	Ser	Leu	Ala	Tyr	Phe	Ser	Cys	Gly	Trp	Tyr	Asn		
	370					375				380							
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Phe Glu Met Pro Leu Gln Lys Met Leu Val Phe Met Met Met His Ala
 385 390 395 400

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 Gln Arg Pro Met Lys Met Arg Ala Leu Leu Val Asp Leu Asn Leu Arg
 405 410 415

 acc ttc ata gac gta agg ctg cta act gct aac tcg ata ttg gat tta 1296
 Thr Phe Ile Asp Val Arg Leu Leu Thr Ala Asn Ser Ile Leu Asp Leu
 420 425 430

 tcg aat tca agc ctt tcc ttt cca gat tgg ccg tgg agc cta cag cta 1344
 Ser Asn Ser Ser Leu Ser Phe Pro Asp Trp Pro Trp Ser Leu Gln Leu
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 ctt caa ttt gct gcg 1359
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 35 40 45

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 Ser Cys Ala Leu Met Leu Ala Arg Val Phe Arg Gly Tyr Glu Asn Leu
 65 70 75 80

 Asn Asp Gly Ala Thr Ser Tyr Ala Thr Ala Val Gln Tyr Phe Ala Val
 85 90 95

 Ser Ile Ala Met Phe Asn Ala Tyr Val Gln Arg Asp Arg Tyr Val Leu
 100 105 110

 Leu Tyr Leu His Ile Val Leu Glu Val Ile Ser Leu Leu Arg Val Ala

115

120

125

His Ser Asp Ile Gln Asn Leu Met His Glu Ala Asp Asn Arg Glu Met
130 135 140

Glu Leu Leu Val Ala Thr Gln Ala Tyr Thr Arg Thr Ile Thr Leu Leu
145 150 155 160

Ile Trp Ile Pro Ser Val Ile Ala Gly Leu Met Ala Tyr Ser Asp Cys
165 170 175

Ile Tyr Arg Ser Leu Phe Leu Pro Lys Ser Val Phe Asn Val Pro Ala
180 185 190

Val	Arg	Arg	Gly	Glu	Glu	His	Pro	Ile	Leu	Leu	Phe	Gln	Leu	Phe	Pro
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Phe Gly Glu Leu Cys Asp Asn Phe Val Val Gly Tyr Leu Gly Pro Trp
210 215 220

Tyr Ala Leu Gly Leu Gly Ile Thr Ala Ile Pro Leu Trp His Thr Phe
225 230 235 240

Ile Thr Cys Leu Met Lys Tyr Val Asn Leu Lys Leu Gln Ile Leu Asn
245 250 255

Lys Arg Val Glu Glu Met Asp Ile Thr Arg Leu Asn Ser Lys Leu Val
260 265 270

Ile Gly Arg Leu Thr Ala Ser Glu Leu Thr Phe Trp Gln Met Gln Leu
275 280 285

Phe Lys Glu Phe Val Lys Glu Gln Leu Arg Ile Arg Lys Phe Val Gln
290 295 300

Glu Leu Gln Tyr Leu Ile Cys Val Pro Val Met Ala Asp Phe Ile Ile
305 310 315 320

Phe Ser Val Leu Ile Cys Phe Leu Phe Phe Ala Leu Thr Val Gly Val
325 330 335

Pro Ser Lys Met Asp Tyr Phe Phe Met Phe Ile Tyr Leu Phe Val Met
340 345 350

Ala Gly Ile Leu Trp Ile Tyr His Trp His Ala Thr Leu Ile Val Glu
355 360 365

Cys His Asp Glu Leu Ser Leu Ala Tyr Phe Ser Cys Gly Trp Tyr Asn

370

375

380

Phe Glu Met Pro Leu Gln Lys Met Leu Val Phe Met Met Met His Ala
385 390 395 400

Gln Arg Pro Met Lys Met Arg Ala Leu Leu Val Asp Leu Asn Leu Arg
405 410 415

Thr Phe Ile Asp Val Arg Leu Leu Thr Ala Asn Ser Ile Leu Asp Leu
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Ser Asn Ser Ser Leu Ser Phe Pro Asp Trp Pro Trp Ser Leu Gln Leu
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Leu Gln Phe Ala Ala
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<213> Drosophila melanogaster

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<223> DOR 69F.1

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gca tgc ata cca aga tat caa tgg aaa gga cgc cct act gaa aga cag 96
Ala Cys Ile Pro Arg Tyr Gln Trp Lys Gly Arg Pro Thr Glu Arg Gln
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ttc tac gct tcg gag caa agg ata gtg ttc ctt ctt gga acc att tgc 144
Phe Tyr Ala Ser Glu Gln Arg Ile Val Phe Leu Leu Gly Thr Ile Cys
35 40 45

cag ata ttc cag att act gga gtg ctt atc tat tgg tat tgc aat ggc 192
Gln Ile Phe Gln Ile Thr Gly Val Leu Ile Tyr Trp Tyr Cys Asn Gly
50 55 60

cgt ctt gcc acg gaa acg ggc acc ttt gtg gca caa tta tct gaa atg 240
Arg Leu Ala Thr Glu Thr Gly Thr Phe Val Ala Gln Leu Ser Glu Met

65

70

75

80

tgc agt tct ttt tgt cta aca ttt gtg gga ttc tgt aac gtt tat gcg 288
Cys Ser Ser Phe Cys Leu Thr Phe Val Gly Phe Cys Asn Val Tyr Ala
85 90 95

atc tct aca aac cgc aat caa att gaa aca tta ctc gag gag ctt cat 336
Ile Ser Thr Asn Arg Asn Gln Ile Glu Thr Leu Leu Glu Glu Leu His
100 105 110

cag ata tat ccg aga tac agg aaa aat cac tat cgc tgc cag cat tat 384
Gln Ile Tyr Pro Arg Tyr Arg Lys Asn His Tyr Arg Cys Gln His Tyr
115 120 125

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Phe Asp Met Ala Met Thr Ile Met Arg Ile Glu Phe Leu Phe Tyr Met
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145 150 155 160

gaa cac ttg cac gag gaa tat gat ctt agc ttc aag acg cag acc aac 528
Glu His Leu His Glu Glu Tyr Asp Leu Ser Phe Lys Thr Gln Thr Asn
165 170 175

act tgg ttt cca tgg aaa gtc cat ggg tcg gca ctt gga ttt ggt atg 576
Thr Trp Phe Pro Trp Lys Val His Gly Ser Ala Leu Gly Phe Gly Met
180 185 190

gct gta cta agc ata acc gtg gga tcc ttt gtg ggc gta ggt ttc agt 624
Ala Val Leu Ser Ile Thr Val Gly Ser Phe Val Gly Val Gly Phe Ser
195 200 205

att gtc acc cag aat ctt atc tgt ttg tta acc ttc caa cta aag ttg 672
Ile Val Thr Gln Asn Leu Ile Cys Leu Leu Thr Phe Gln Leu Lys Leu
210 215 220

cac tac gat gga ata tcc agt cag tta gta tct ctc gat tgc cgt cgt 720
His Tyr Asp Gly Ile Ser Ser Gln Leu Val Ser Leu Asp Cys Arg Arg
225 230 235 240

cct gga gct cat aag gag ttg agc atc ctc atc gcc cac cac agc cga 768
Pro Gly Ala His Lys Glu Leu Ser Ile Leu Ile Ala His His Ser Arg
245 250 255

atc ctt cag ctg ggc gac caa gtc aat gac ata atg aac ttt gta ttc 816
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35 40 45

Gln Ile Phe Gln Ile Thr Gly Val Leu Ile Tyr Trp Tyr Cys Asn Gly
50 55 60

Arg Leu Ala Thr Glu Thr Gly Thr Phe Val Ala Gln Leu Ser Glu Met
65 70 75 80

Cys Ser Ser Phe Cys Leu Thr Phe Val Gly Phe Cys Asn Val Tyr Ala
85 90 95

Ile Ser Thr Asn Arg Asn Gln Ile Glu Thr Leu Leu Glu Glu Leu His
100 105 110

Gln Ile Tyr Pro Arg Tyr Arg Lys Asn His Tyr Arg Cys Gln His Tyr
115 120 125

Phe Asp Met Ala Met Thr Ile Met Arg Ile Glu Phe Leu Phe Tyr Met
130 135 140

Ile Leu Tyr Val Tyr Tyr Asn Ser Ala Pro Leu Trp Val Leu Leu Trp
145 150 155 160

Glu His Leu His Glu Glu Tyr Asp Leu Ser Phe Lys Thr Gln Thr Asn
165 170 175

Thr Trp Phe Pro Trp Lys Val His Gly Ser Ala Leu Gly Phe Gly Met
180 185 190

Ala Val Leu Ser Ile Thr Val Gly Ser Phe Val Gly Val Gly Phe Ser
195 200 205

Ile Val Thr Gln Asn Leu Ile Cys Leu Leu Thr Phe Gln Leu Lys Leu
210 215 220

His Tyr Asp Gly Ile Ser Ser Gln Leu Val Ser Leu Asp Cys Arg Arg
225 230 235 240

Pro Gly Ala His Lys Glu Leu Ser Ile Leu Ile Ala His His Ser Arg
245 250 255

Met	Gln	Leu	Glu	Asp	Phe	Met	Arg	Tyr	Pro	Asp	Leu	Val	Cys	Gln	Ala		
1				5					10					15			
gcc caa ctt ccc aga tac acg tgg aat ggc aga cga tcc ttg gaa gtt 96																	
Ala	Gln	Leu	Pro	Arg	Tyr	Thr	Trp	Asn	Gly	Arg	Arg	Ser	Leu	Glu	Val		
		20						25					30				
aaa cgc aac ttg gca aaa cgc att atc ttc tgg ctt gga gca gta aat 144																	
Lys	Arg	Asn	Leu	Ala	Lys	Arg	Ile	Ile	Phe	Trp	Leu	Gly	Ala	Val	Asn		
		35					40					45					
ttg gtt tat cac aat att ggc tgc gtc atg tat ggc tat ttc ggt gat 192																	
Leu	Val	Tyr	His	Asn	Ile	Gly	Cys	Val	Met	Tyr	Gly	Tyr	Phe	Gly	Asp		
		50				55					60						
gga aga aca aag gat cca att gcg tat tta gct gaa ttg gca tct gtg 240																	
Gly	Arg	Thr	Lys	Asp	Pro	Ile	Ala	Tyr	Leu	Ala	Glu	Leu	Ala	Ser	Val		
	65				70				75					80			
gcc agc atg ctt ggt ttc acc att gtg ggc acc ctc aac ttg tgg aag 288																	
Ala	Ser	Met	Leu	Gly	Phe	Thr	Ile	Val	Gly	Thr	Leu	Asn	Leu	Trp	Lys		
			85					90					95				
atg ctg agc ctt aag acc cat ttt gag aac cta cta aat gaa ttc gag 336																	
Met	Leu	Ser	Leu	Lys	Thr	His	Phe	Glu	Asn	Leu	Leu	Asn	Glu	Phe	Glu		
			100					105					110				
gaa tta ttt caa cta atc aag cac agg gcg tat cgc ata cac cac tat 384																	
Glu	Leu	Phe	Gln	Leu	Ile	Lys	His	Arg	Ala	Tyr	Arg	Ile	His	His	Tyr		
		115				120						125					
caa gaa aag tat acg cgt cat ata cga aat aca ttt att ttc cat acc 432																	
Gln	Glu	Lys	Tyr	Thr	Arg	His	Ile	Arg	Asn	Thr	Phe	Ile	Phe	His	Thr		
		130				135					140						
tct gcc gtt gtc tac tac aac tca cta cca att ctt cta atg att cgg 480																	
Ser	Ala	Val	Val	Tyr	Tyr	Asn	Ser	Leu	Pro	Ile	Leu	Leu	Met	Ile	Arg		
	145				150				155				160				
gaa cat ttc tcg aac tca cag cag ttg ggc tat aga att cag agt aat 528																	
Glu	His	Phe	Ser	Asn	Ser	Gln	Gln	Leu	Gly	Tyr	Arg	Ile	Gln	Ser	Asn		
			165					170				175					
acc tgg tat ccc tgg cag gtt cag gga tca att cct gga ttt ttt gct 576																	
Thr	Trp	Tyr	Pro	Trp	Gln	Val	Gln	Gly	Ser	Ile	Pro	Gly	Phe	Phe	Ala		
			180				185					190					
gca gtc gcc tgt caa atc ttt tcg tgc caa acc aat atg tgc gtc aat 624																	

Trp His Leu Leu Phe Asn Phe Asn Ser Cys Val Gly Phe Gln Thr Leu
 385 390 395 400

aag ttt tca tat caa atg ttt acc tgt gtg cgg tcc ctt aaa 1242
 Lys Phe Ser Tyr Gln Met Phe Thr Cys Val Arg Ser Leu Lys
 405 410

<210> 48
 <211> 414
 <212> PRT
 <213> Drosophila melanogaster

<400> 48
 Met Gln Leu Glu Asp Phe Met Arg Tyr Pro Asp Leu Val Cys Gln Ala
 1 5 10 15

Ala Gln Leu Pro Arg Tyr Thr Trp Asn Gly Arg Arg Ser Leu Glu Val
 20 25 30

Lys Arg Asn Leu Ala Lys Arg Ile Ile Phe Trp Leu Gly Ala Val Asn
 35 40 45

Leu Val Tyr His Asn Ile Gly Cys Val Met Tyr Gly Tyr Phe Gly Asp
 50 55 60

Gly Arg Thr Lys Asp Pro Ile Ala Tyr Leu Ala Glu Leu Ala Ser Val
 65 70 75 80

Ala Ser Met Leu Gly Phe Thr Ile Val Gly Thr Leu Asn Leu Trp Lys
 85 90 95

Met Leu Ser Leu Lys Thr His Phe Glu Asn Leu Leu Asn Glu Phe Glu
 100 105 110

Glu Leu Phe Gln Leu Ile Lys His Arg Ala Tyr Arg Ile His His Tyr
 115 120 125

Gln Glu Lys Tyr Thr Arg His Ile Arg Asn Thr Phe Ile Phe His Thr
 130 135 140

Ser Ala Val Val Tyr Tyr Asn Ser Leu Pro Ile Leu Leu Met Ile Arg
 145 150 155 160

Glu His Phe Ser Asn Ser Gln Gln Leu Gly Tyr Arg Ile Gln Ser Asn
 165 170 175

Thr Trp Tyr Pro Trp Gln Val Gln Gly Ser Ile Pro Gly Phe Phe Ala

gtg gtg ggc aaa cag ttg ccg tac ctc atg tac att cct tgg aaa tgg	528
Val Val Gly Lys Gln Leu Pro Tyr Leu Met Tyr Ile Pro Trp Lys Trp	
165 170 175	
cag gat aac tgg tcg tac tat cca ctg tta ttc tcc cag aat ttt gca	576
Gln Asp Asn Trp Ser Tyr Tyr Pro Leu Leu Phe Ser Gln Asn Phe Ala	
180 185 190	
gga tac aca tct gca gct ggt caa att tca acc gat gtc ttg ctc tgc	624
Gly Tyr Thr Ser Ala Ala Gly Gln Ile Ser Thr Asp Val Leu Leu Cys	
195 200 205	
gcg gtg gcc act cag ttg gta atg cac ttc gac ttt ctc tca aat agt	672
Ala Val Ala Thr Gln Leu Val Met His Phe Asp Phe Leu Ser Asn Ser	
210 215 220	
atg gaa cgc cac gaa ttg agt gga gat tgg aag aag gac tcc cga ttt	720
Met Glu Arg His Glu Leu Ser Gly Asp Trp Lys Lys Asp Ser Arg Phe	
225 230 235 240	
ctg gtg gac att gtt agg tat cac gaa cgt ata ctc cgc ctt tca gat	768
Leu Val Asp Ile Val Arg Tyr His Glu Arg Ile Leu Arg Leu Ser Asp	
245 250 255	
gca gtg aac gat ata ttt gga att cca cta cta ctc aac ttc atg gta	816
Ala Val Asn Asp Ile Phe Gly Ile Pro Leu Leu Leu Asn Phe Met Val	
260 265 270	
tcc tcg ttc gtc atc tgc ttc gtg gga ttc cag atg act gtt gga gtt	864
Ser Ser Phe Val Ile Cys Phe Val Gly Phe Gln Met Thr Val Gly Val	
275 280 285	
ccg ccg gat ata gtt gtg aag ctc ttc ctc ttc ctt gtc tct tcg atg	912
Pro Pro Asp Ile Val Val Lys Leu Phe Leu Phe Leu Val Ser Ser Met	
290 295 300	
agt cag gtc tat ttg att tgt cac tat ggt caa ctg gtg gcc gat gct	960
Ser Gln Val Tyr Leu Ile Cys His Tyr Gly Gln Leu Val Ala Asp Ala	
305 310 315 320	
agc tac gga ttt tcg gtt gcc acc tac aat cag aag tgg tat aaa gcc	1008
Ser Tyr Gly Phe Ser Val Ala Thr Tyr Asn Gln Lys Trp Tyr Lys Ala	
325 330 335	
gat gtg cgc tat aaa cga gcc ttg gtt att att ata gct aga tcg cag	1056
Asp Val Arg Tyr Lys Arg Ala Leu Val Ile Ile Ile Ala Arg Ser Gln	
340 345 350	

aag gta act ttt cta aag gcc act ata ttc ttg gat att acc agg tcc 1104
 Lys Val Thr Phe Leu Lys Ala Thr Ile Phe Leu Asp Ile Thr Arg Ser
 355 360 365

act atg aca gat ctg ctt caa ata tca tac aaa ttc ttc gcc ctg ctg 1152
 Thr Met Thr Asp Leu Leu Gln Ile Ser Tyr Lys Phe Phe Ala Leu Leu
 370 375 380

cgc aca atg tat acc caa 1170
 Arg Thr Met Tyr Thr Gln
 385 390

<210> 50
 <211> 390
 <212> PRT
 <213> Drosophila melanogaster

<400> 50
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 1 5 10 15

Tyr Gly His Ile Pro Met Gly Glu Glu Ser Lys Arg Asn Lys Leu Ile
 20 25 30

Phe His Ile Val Phe Trp Ser Asn Val Ile Asn Leu Ser Phe Val Gly
 35 40 45

Leu Phe Glu Ser Ile Tyr Val Tyr Ser Ala Phe Met Asp Asn Lys Phe
 50 55 60

Leu Glu Ala Val Thr Ala Leu Ser Tyr Ile Gly Phe Val Thr Val Gly
 65 70 75 80

Met Ser Lys Met Phe Phe Ile Arg Trp Lys Lys Thr Ala Ile Thr Glu
 85 90 95

Leu Ile Asn Glu Leu Lys Glu Ile Tyr Pro Asn Gly Leu Ile Arg Glu
 100 105 110

Glu Arg Tyr Asn Leu Pro Met Tyr Leu Gly Thr Cys Ser Arg Ile Ser
 115 120 125

Leu Ile Tyr Ser Leu Leu Tyr Ser Val Leu Ile Trp Thr Phe Asn Leu
 130 135 140

Phe Cys Val Met Glu Tyr Trp Val Tyr Asp Lys Trp Leu Asn Ile Arg

<210> 51
 <211> 1167
 <212> DNA
 <213> Drosophila melanogaster

<220>
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 <222> (1)..(1167).
 <223> DOR 85A.3

<400> 51
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 Met Lys Phe Met Lys Tyr Ala Val Phe Phe Tyr Thr Ser Val Gly Ile
 1 5 10 15

gag ccg tat acg att gac tcg cgg tcc aaa aaa gcg agc cta tgg tca 96
 Glu Pro Tyr Thr Ile Asp Ser Arg Ser Lys Lys Ala Ser Leu Trp Ser
 20 25 30

cat ctt ctc ttc tgg gcc aat gtg atc aat tta agt gtc att gtt ttc 144
 His Leu Leu Phe Trp Ala Asn Val Ile Asn Leu Ser Val Ile Val Phe
 35 40 45

gga gag atc ctc tat ctg gga gtg gcc tat tcc gat gga aag ttc att 192
 Gly Glu Ile Leu Tyr Leu Gly Val Ala Tyr Ser Asp Gly Lys Phe Ile
 50 55 60

gat gcc gtc act gta ctg tca tat atc gga ttc gta atc gtg ggc atg 240
 Asp Ala Val Thr Val Leu Ser Tyr Ile Gly Phe Val Ile Val Gly Met
 65 70 75 80

agc aag atg ttc ttc ata tgg tgg aag aag acc gat cta agc gat ttg 288
 Ser Lys Met Phe Phe Ile Trp Trp Lys Lys Thr Asp Leu Ser Asp Leu
 85 90 95

gtt aag gaa ttg gag cac atc tat cca aat ggc aaa gct gag gag gag 336
 Val Lys Glu Leu Glu His Ile Tyr Pro Asn Gly Lys Ala Glu Glu Glu
 100 105 110

atg tat cgg ttg gat agg tat ctg cga tct tgt tca cga att agc att 384
 Met Tyr Arg Leu Asp Arg Tyr Leu Arg Ser Cys Ser Arg Ile Ser Ile
 115 120 125

acc tat gca cta ctc tac tcc gta ctc atc tgg acc ttc aat ctg ttc 432
 Thr Tyr Ala Leu Leu Tyr Ser Val Leu Ile Trp Thr Phe Asn Leu Phe
 130 135 140

130

135

140

Ser Ile Met Gln Phe Leu Val Tyr Glu Lys Leu Leu Lys Ile Arg Val
 145 150 155 160

Val Gly Gln Thr Leu Pro Tyr Leu Met Tyr Phe Pro Trp Asn Trp His
 165 170 175

Glu Asn Trp Thr Tyr Tyr Val Leu Leu Phe Cys Gln Asn Phe Ala Gly
 180 185 190

His Thr Ser Ala Ser Gly Gln Ile Ser Thr Asp Leu Leu Leu Cys Ala
 195 200 205

Val Ala Thr Gln Val Val Met His Phe Asp Tyr Leu Ala Arg Val Val
 210 215 220

Glu Lys Gln Val Leu Asp Arg Asp Trp Ser Glu Asn Ser Arg Phe Leu
 225 230 235 240

Ala Lys Thr Val Gln Tyr His Gln Arg Ile Leu Arg Leu Met Asp Val
 245 250 255

Leu Asn Asp Ile Phe Gly Ile Pro Leu Leu Leu Asn Phe Met Val Ser
 260 265 270

Thr Phe Val Ile Cys Phe Val Gly Phe Gln Met Thr Val Gly Val Pro
 275 280 285

Pro Asp Ile Met Ile Lys Leu Phe Leu Phe Leu Phe Ser Ser Leu Ser
 290 295 300

Gln Val Tyr Leu Ile Cys His Tyr Gly Gln Leu Ile Ala Asp Ala Ser
 305 310 315 320

Ser Ser Leu Ser Ile Ser Ala Tyr Lys Gln Asn Trp Gln Asn Ala Asp
 325 330 335

Ile Arg Tyr Arg Arg Ala Leu Val Phe Phe Ile Ala Arg Pro Gln Arg
 340 345 350

Thr Thr Tyr Leu Lys Ala Thr Ile Phe Met Asn Ile Thr Arg Ala Thr
 355 360 365

Met Thr Asp Leu Leu Gln Val Ser Tyr Lys Phe Phe Ala Leu Leu Arg
 370 375 380

Thr Met Tyr Ile Lys

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 <212> DNA
 <213> Drosophila melanogaster

<220>
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 <222> (1)..(1305)
 <223> DOR 85B.1

<400> 53
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 Met Gly Leu Gln Leu Ala Asn Gly Thr Lys Pro Ser Pro Arg Leu Pro
 1 5 10 15

aaa tgg tgg cca aag cgg ctg gaa atg att ggt aaa gtg ctg ccc aaa 96
 Lys Trp Trp Pro Lys Arg Leu Glu Met Ile Gly Lys Val Leu Pro Lys
 20 25 30

gcc tat tgt tcc atg gtg att ttc acc tcc ctg cat ttg ggt gtc ctg 144
 Ala Tyr Cys Ser Met Val Ile Phe Thr Ser Leu His Leu Gly Val Leu
 35 40 45

ttc acg aaa acc aca ctg gat gtc ctg ccg acg ggg gag ctg cag gcc 192
 Phe Thr Lys Thr Thr Leu Asp Val Leu Pro Thr Gly Glu Leu Gln Ala
 50 55 60

ata acg gat gcc ctc acc atg acc ata ata tac ttt ttc acg ggc tac 240
 Ile Thr Asp Ala Leu Thr Met Thr Ile Ile Tyr Phe Phe Thr Gly Tyr
 65 70 75 80

ggc acc atc tac tgg tgc ctg cgc tcc cgg cgc ctc ttg gcc tac atg 288
 Gly Thr Ile Tyr Trp Cys Leu Arg Ser Arg Arg Leu Leu Ala Tyr Met
 85 90 95

gag cac atg aac cgg gag tat cgc cat cat tcg ctg gcc ggg gtg acc 336
 Glu His Met Asn Arg Glu Tyr Arg His His Ser Leu Ala Gly Val Thr
 100 105 110

ttt gtg agt agc cat gcg gcc ttt agg atg tcc aga aac ttc acg gtg 384
 Phe Val Ser Ser His Ala Ala Phe Arg Met Ser Arg Asn Phe Thr Val
 115 120 125

gtg tgg ata atg tcc tgc ctg ctg ggc gtg att tcc tgg ggc gtt tcg 432

Val Trp Ile Met Ser Cys Leu Leu Gly Val Ile Ser Trp Gly Val Ser
 130 135 140

cca ctg atg ctg ggc atc cgg atg ctg ccg ctc caa tgt tgg tat ccc 480
 Pro Leu Met Leu Gly Ile Arg Met Leu Pro Leu Gln Cys Trp Tyr Pro
 145 150 155 160

ttc gac gcc ctg ggt ccc ggc aca tat acg gcg gtc tat gct aca caa 528
 Phe Asp Ala Leu Gly Pro Gly Thr Tyr Thr Ala Val Tyr Ala Thr Gln
 165 170 175

ctt ttc ggt cag atc atg gtg ggc atg acc ttt gga ttc ggg gga tca 576
 Leu Phe Gly Gln Ile Met Val Gly Met Thr Phe Gly Phe Gly Gly Ser
 180 185 190

ctg ttt gtc acc ctg agc ctg cta ctc ctg gga caa ttc gat gtg ctc 624
 Leu Phe Val Thr Leu Ser Leu Leu Leu Leu Gly Gln Phe Asp Val Leu
 195 200 205

tac tgc agc ctg aag aac ctg gat gcc cat acc aag ttg ctg ggc ggg 672
 Tyr Cys Ser Leu Lys Asn Leu Asp Ala His Thr Lys Leu Leu Gly Gly
 210 215 220

gag tct gta aat ggc ctg agt tcg ctg caa gag gag ttg ctg ctg ggg 720
 Glu Ser Val Asn Gly Leu Ser Ser Leu Gln Glu Glu Leu Leu Leu Gly
 225 230 235 240

gac tcg aag agg gaa tta aat cag tac gtt ttg ctc cag gag cat ccg 768
 Asp Ser Lys Arg Glu Leu Asn Gln Tyr Val Leu Leu Gln Glu His Pro
 245 250 255

acg gat ctg ctg aga ttg tcg gca gga cga aaa tgt cct gac caa gga 816
 Thr Asp Leu Leu Arg Leu Ser Ala Gly Arg Lys Cys Pro Asp Gln Gly
 260 265 270

aat gcg ttt cac aac gcc ttg gtg gaa tgc att cgc ttg cat cgc ttc 864
 Asn Ala Phe His Asn Ala Leu Val Glu Cys Ile Arg Leu His Arg Phe
 275 280 285

att ctg cac tgc tca cag gag ttg gag aat cta ttc agt cca tat tgt 912
 Ile Leu His Cys Ser Gln Glu Leu Glu Asn Leu Phe Ser Pro Tyr Cys
 290 295 300

ctg gtc aag tca ctg cag atc acc ttt cag ctt tgc ctg ctg gtc ttt 960
 Leu Val Lys Ser Leu Gln Ile Thr Phe Gln Leu Cys Leu Leu Val Phe
 305 310 315 320

gtg ggc gtt tcg ggt act cga gag gtc ctg cgg att gtc aac cag cta 1008

Val Gly Val Ser Gly Thr Arg Glu Val Leu Arg Ile Val Asn Gln Leu
 325 330 335

cag tac ttg gga ctg acc atc ttc gag ctc cta atg ttc acc tat tgt 1056
 Gln Tyr Leu Gly Leu Thr Ile Phe Glu Leu Leu Met Phe Thr Tyr Cys
 340 345 350

ggc gaa ctc ctc agt cgg cat agt att cga tct ggc gac gcc ttt tgg 1104
 Gly Glu Leu Leu Ser Arg His Ser Ile Arg Ser Gly Asp Ala Phe Trp
 355 360 365

agg ggt gcg tgg tgg aag cac gcc cat ttc atc cgc cag gac atc ctc 1152
 Arg Gly Ala Trp Trp Lys His Ala His Phe Ile Arg Gln Asp Ile Leu
 370 375 380

atc ttt ctg gtc aat agt aga cgt gca gtt cac gtg act gcc ggc aag 1200
 Ile Phe Leu Val Asn Ser Arg Arg Ala Val His Val Thr Ala Gly Lys
 385 390 395 400

ttt tat gtg atg gat gtg aat cgt cta aga tcg gtt ata acg cag gcg 1248
 Phe Tyr Val Met Asp Val Asn Arg Leu Arg Ser Val Ile Thr Gln Ala
 405 410 415

ttc agc ttc ttg act ttg ctg caa aag ttg gct gcc aag aag acg gaa 1296
 Phe Ser Phe Leu Thr Leu Leu Gln Lys Leu Ala Ala Lys Lys Thr Glu
 420 425 430

tcg gag ctc 1305
 Ser Glu Leu
 435

<210> 54

<211> 435

<212> PRT

<213> Drosophila melanogaster

<400> 54

Met Gly Leu Gln Leu Ala Asn Gly Thr Lys Pro Ser Pro Arg Leu Pro
 1 5 10 15

Lys Trp Trp Pro Lys Arg Leu Glu Met Ile Gly Lys Val Leu Pro Lys
 20 25 30

Ala Tyr Cys Ser Met Val Ile Phe Thr Ser Leu His Leu Gly Val Leu
 35 40 45

Phe Thr Lys Thr Thr Leu Asp Val Leu Pro Thr Gly Glu Leu Gln Ala

60

Leu Val Lys Ser Leu Gln Ile Thr Phe Gln Leu Cys Leu Leu Val Phe

305 310 315 320
 Val Gly Val Ser Gly Thr Arg Glu Val Leu Arg Ile Val Asn Gln Leu
 325 330 335
 Gln Tyr Leu Gly Leu Thr Ile Phe Glu Leu Leu Met Phe Thr Tyr Cys
 340 345 350
 Gly Glu Leu Leu Ser Arg His Ser Ile Arg Ser Gly Asp Ala Phe Trp
 355 360 365
 Arg Gly Ala Trp Trp Lys His Ala His Phe Ile Arg Gln Asp Ile Leu
 370 375 380
 Ile Phe Leu Val Asn Ser Arg Arg Ala Val His Val Thr Ala Gly Lys
 385 390 395 400
 Phe Tyr Val Met Asp Val Asn Arg Leu Arg Ser Val Ile Thr Gln Ala
 405 410 415
 Phe Ser Phe Leu Thr Leu Leu Gln Lys Leu Ala Ala Lys Lys Thr Glu
 420 425 430
 Ser Glu Leu
 435

<210> 55
 <211> 1203
 <212> DNA
 <213> Drosophila melanogaster

<220>
 <221> CDS
 <222> (1)..(1203)

<400> 55
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 Met Lys Pro Thr Glu Ile Lys Lys Pro Tyr Arg Met Glu Glu Phe Leu
 1 5 10 15

 cgt ccg cag atg ttc cag gag gtg gct cag atg gtg cat ttc cag tgg 96
 Arg Pro Gln Met Phe Gln Glu Val Ala Gln Met Val His Phe Gln Trp
 20 25 30

 cgg aga aat ccg gtg gac aac agc atg gtg aac gca tcc atg gtc ccc 144
 Arg Arg Asn Pro Val Asp Asn Ser Met Val Asn Ala Ser Met Val Pro

35

40

45

ttc tgc ttg tgc gcg ttt ctt aat gtc ctg ttt ttc ggc tgc aat ggt 192
 Phe Cys Leu Ser Ala Phe Leu Asn Val Leu Phe Phe Gly Cys Asn Gly
 50 55 60

tgg gac atc ata gga cat ttt tgg ctg gga cat cct gcc aac cag aat 240
 Trp Asp Ile Ile Gly His Phe Trp Leu Gly His Pro Ala Asn Gln Asn
 65 70 75 80

ccg ccc gtg ott agc atc acc att tac ttc tgc atc agg gga ttg atg 288
 Pro Pro Val Leu Ser Ile Thr Ile Tyr Phe Ser Ile Arg Gly Leu Met
 85 90 95

cta tac ctg aaa cga aag gaa atc gtt gag ttt gtt aac gac ttg gat 336
 Leu Tyr Leu Lys Arg Lys Glu Ile Val Glu Phe Val Asn Asp Leu Asp
 100 105 110

cgg gag tgt ccg cgg gac ttg gtc agc cag ttg gac atg caa atg gat 384
 Arg Glu Cys Pro Arg Asp Leu Val Ser Gln Leu Asp Met Gln Met Asp
 115 120 125

gag acg tac cga aac ttt tgg cag cgc tat cgc ttc atc cgt atc tac 432
 Glu Thr Tyr Arg Asn Phe Trp Gln Arg Tyr Arg Phe Ile Arg Ile Tyr
 130 135 140

tcc cat ttg ggt ggt ccg atg ttc tgc gtt gtg cca tta gct cta ttc 480
 Ser His Leu Gly Gly Pro Met Phe Cys Val Val Pro Leu Ala Leu Phe
 145 150 155 160

ctc ctg acc cac gag ggt aaa gat act cct gtt gcc cag cac gag cag 528
 Leu Leu Thr His Glu Gly Lys Asp Thr Pro Val Ala Gln His Glu Gln
 165 170 175

ctc ctt gga gga tgg ctg cca tgc ggt gtg cga aag gac cca aat ttc 576
 Leu Leu Gly Gly Trp Leu Pro Cys Gly Val Arg Lys Asp Pro Asn Phe
 180 185 190

tac ctt tta gtc tgg tcc ttc gac ctg atg tgc acc act tgc ggc gtc 624
 Tyr Leu Leu Val Trp Ser Phe Asp Leu Met Cys Thr Thr Cys Gly Val
 195 200 205

tcc ttt ttc gtt acc ttc gac aac cta ttc aat gtg atg cag gga cat 672
 Ser Phe Phe Val Thr Phe Asp Asn Leu Phe Asn Val Met Gln Gly His
 210 215 220

ttg gtc atg cat ttg ggc cat ctt gct cgc cag ttt tgc gcc atc gat 720
 Leu Val Met His Leu Gly His Leu Ala Arg Gln Phe Ser Ala Ile Asp

225	230	235	240	
cct cga cag agt ttg acc gat gag aag cga ttc ttt gtg gat ctt agg				768
Pro Arg Gln Ser Leu Thr Asp Glu Lys Arg Phe Phe Val Asp Leu Arg				
245		250	255	
tta tta gtt cag agg cag cag ctt ctt aat gga ttg tgc aga aaa tac				816
Leu Leu Val Gln Arg Gln Gln Leu Leu Asn Gly Leu Cys Arg Lys Tyr				
260		265	270	
aac gac atc ttt aaa gtg gcc ttc ctg gtg agc aat ttt gta ggc gcc				864
Asn Asp Ile Phe Lys Val Ala Phe Leu Val Ser Asn Phe Val Gly Ala				
275		280	285	
ggt tcc ctc tgc ttc tac ctc ttt atg ctc tcg gag aca tca gat gtc				912
Gly Ser Leu Cys Phe Tyr Leu Phe Met Leu Ser Glu Thr Ser Asp Val				
290		295	300	
ctt atc atc gcc cag tat ata tta ccc act ttg gtc ctg gtg ggc ttc				960
Leu Ile Ile Ala Gln Tyr Ile Leu Pro Thr Leu Val Leu Val Gly Phe				
305		310	315	320
aca ttt gag att tgt cta cgg gga acc caa ctg gaa aag gcg tcg gag				1008
Thr Phe Glu Ile Cys Leu Arg Gly Thr Gln Leu Glu Lys Ala Ser Glu				
325		330	335	
gga ctg gaa tcg tcg ttg cga agc cag gaa tgg tat ttg gga agt agg				1056
Gly Leu Glu Ser Ser Leu Arg Ser Gln Glu Trp Tyr Leu Gly Ser Arg				
340		345	350	
cgg tac cgg aag ttc tat ttg ctc tgg acg caa tat tgc cag cga aca				1104
Arg Tyr Arg Lys Phe Tyr Leu Leu Trp Thr Gln Tyr Cys Gln Arg Thr				
355		360	365	
cag caa ctg ggc gcc ttt ggg cta atc caa gtc aat atg gtg cac ttc				1152
Gln Gln Leu Gly Ala Phe Gly Leu Ile Gln Val Asn Met Val His Phe				
370		375	380	
act gaa ata atg cag ctg gcc tat aga ctc ttc act ttt ctc aaa tct				1200
Thr Glu Ile Met Gln Leu Ala Tyr Arg Leu Phe Thr Phe Leu Lys Ser				
385		390	395	400
cat				1203
His				

<210> 56

<211> 401

<212> PRT

<213> Drosophila melanogaster

<400> 56

Met Lys Pro Thr Glu Ile Lys Lys Pro Tyr Arg Met Glu Glu Phe Leu
1 5 10 15

Arg Pro Gln Met Phe Gln Glu Val Ala Gln Met Val His Phe Gln Trp
20 25 30

Arg Arg Asn Pro Val Asp Asn Ser Met Val Asn Ala Ser Met Val Pro
35 40 45

Phe Cys Leu Ser Ala Phe Leu Asn Val Leu Phe Phe Gly Cys Asn Gly
50 55 60

Trp Asp Ile Ile Gly His Phe Trp Leu Gly His Pro Ala Asn Gln Asn
65 70 75 80

Pro Pro Val Leu Ser Ile Thr Ile Tyr Phe Ser Ile Arg Gly Leu Met
85 90 95

Leu Tyr Leu Lys Arg Lys Glu Ile Val Glu Phe Val Asn Asp Leu Asp
100 105 110

Arg Glu Cys Pro Arg Asp Leu Val Ser Gln Leu Asp Met Gln Met Asp
115 120 125

Glu Thr Tyr Arg Asn Phe Trp Gln Arg Tyr Arg Phe Ile Arg Ile Tyr
130 135 140

Ser His Leu Gly Gly Pro Met Phe Cys Val Val Pro Leu Ala Leu Phe
145 150 155 160

Leu Leu Thr His Glu Gly Lys Asp Thr Pro Val Ala Gln His Glu Gln
165 170 175

Leu Leu Gly Gly Trp Leu Pro Cys Gly Val Arg Lys Asp Pro Asn Phe
180 185 190

Tyr Leu Leu Val Trp Ser Phe Asp Leu Met Cys Thr Thr Cys Gly Val
195 200 205

Ser Phe Phe Val Thr Phe Asp Asn Leu Phe Asn Val Met Gln Gly His
210 215 220

Leu Val Met His Leu Gly His Leu Ala Arg Gln Phe Ser Ala Ile Asp
225 230 235 240

Pro Arg Gln Ser Leu Thr Asp Glu Lys Arg Phe Phe Val Asp Leu Arg
 245 250 255

Leu Leu Val Gln Arg Gln Gln Leu Leu Asn Gly Leu Cys Arg Lys Tyr
 260 265 270

Asn Asp Ile Phe Lys Val Ala Phe Leu Val Ser Asn Phe Val Gly Ala
 275 280 285

Gly Ser Leu Cys Phe Tyr Leu Phe Met Leu Ser Glu Thr Ser Asp Val
 290 295 300

Leu Ile Ile Ala Gln Tyr Ile Leu Pro Thr Leu Val Leu Val Gly Phe
 305 310 315 320

Thr Phe Glu Ile Cys Leu Arg Gly Thr Gln Leu Glu Lys Ala Ser Glu
 325 330 335

Gly Leu Glu Ser Ser Leu Arg Ser Gln Glu Trp Tyr Leu Gly Ser Arg
 340 345 350

Arg Tyr Arg Lys Phe Tyr Leu Leu Trp Thr Gln Tyr Cys Gln Arg Thr
 355 360 365

Gln Gln Leu Gly Ala Phe Gly Leu Ile Gln Val Asn Met Val His Phe
 370 375 380

Thr Glu Ile Met Gln Leu Ala Tyr Arg Leu Phe Thr Phe Leu Lys Ser
 385 390 395 400

His

<210> 57

<211> 1131

<212> DNA

<213> Drosophila melanogaster

<220>

<221> CDS

<222> (1)..(1131)

<223> DOR 92E.1

<400> 57

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1				5					10						15		
ccg	aat	gtg	ata	agg	cgt	tac	ctg	cta	cgt	ttt	tat	ctg	gta	ctc	ggg	96	
Pro	Asn	Val	Ile	Arg	Arg	Tyr	Leu	Leu	Arg	Phe	Tyr	Leu	Val	Leu	Gly		
			20					25					30				
ttt	ctc	aac	ttc	aat	gcc	tat	gtg	gtg	ggc	gaa	atc	gcg	tac	ttt	ata	144	
Phe	Leu	Asn	Phe	Asn	Ala	Tyr	Val	Val	Gly	Glu	Ile	Ala	Tyr	Phe	Ile		
		35					40					45					
gtc	cat	ata	atg	tcg	acg	act	act	ctt	ttg	gag	gcc	act	gca	gtg	gca	192	
Val	His	Ile	Met	Ser	Thr	Thr	Thr	Leu	Leu	Glu	Ala	Thr	Ala	Val	Ala		
	50					55					60						
ccg	tgc	att	ggg	ttc	agc	ttc	atg	gcc	gac	ttt	aag	cag	ttc	ggg	ctc	240	
Pro	Cys	Ile	Gly	Phe	Ser	Phe	Met	Ala	Asp	Phe	Lys	Gln	Phe	Gly	Leu		
	65				70					75					80		
aca	gtg	aat	aga	aag	cga	ttg	gtc	aga	ttg	ctg	gat	gat	ctc	aag	gag	288	
Thr	Val	Asn	Arg	Lys	Arg	Leu	Val	Arg	Leu	Leu	Asp	Asp	Leu	Lys	Glu		
				85				90						95			
ata	ttt	cct	tta	gat	tta	gaa	gcg	cag	cgg	aag	tat	aac	gta	tcg	ttt	336	
Ile	Phe	Pro	Leu	Asp	Leu	Glu	Ala	Gln	Arg	Lys	Tyr	Asn	Val	Ser	Phe		
			100					105					110				
tac	cgg	aaa	cac	atg	aac	agg	gtc	atg	acc	cta	ttc	acc	atc	ctc	tgc	384	
Tyr	Arg	Lys	His	Met	Asn	Arg	Val	Met	Thr	Leu	Phe	Thr	Ile	Leu	Cys		
		115					120					125					
atg	acc	tac	acc	tcg	tca	ttt	agc	ttt	tat	cca	gcc	atc	aag	tcg	acc	432	
Met	Thr	Tyr	Thr	Ser	Ser	Phe	Ser	Phe	Tyr	Pro	Ala	Ile	Lys	Ser	Thr		
	130					135					140						
ata	aag	tat	tac	ctt	atg	gga	tcg	gaa	atc	ttt	gag	cgc	aac	tac	gga	480	
Ile	Lys	Tyr	Tyr	Leu	Met	Gly	Ser	Glu	Ile	Phe	Glu	Arg	Asn	Tyr	Gly		
	145				150				155						160		
ttt	cac	att	ttg	ttt	ccc	tac	gac	gca	gaa	acg	gat	ctg	acg	gtc	tac	528	
Phe	His	Ile	Leu	Phe	Pro	Tyr	Asp	Ala	Glu	Thr	Asp	Leu	Thr	Val	Tyr		
			165					170						175			
tgg	ttt	tcc	tac	tgg	gga	ttg	gct	cat	tgt	gcc	tat	gtg	gcc	gga	gtt	576	
Trp	Phe	Ser	Tyr	Trp	Gly	Leu	Ala	His	Cys	Ala	Tyr	Val	Ala	Gly	Val		
			180					185					190				
tcc	tac	gtc	tgc	gtg	gat	ctc	ctg	ctg	atc	gcg	acc	ata	acc	cag	ctg	624	

Ser Tyr Val Cys Val Asp Leu Leu Leu Ile Ala Thr Ile Thr Gln Leu
 195 200 205

acc atg cac ttc aac ttt ata gcg aat gat ttg gag gcc tac gaa gga 672
 Thr Met His Phe Asn Phe Ile Ala Asn Asp Leu Glu Ala Tyr Glu Gly
 210 215 220

ggt gat cat acg gat gaa gaa aat atc aaa tac ctg cac aac ttg gtc 720
 Gly Asp His Thr Asp Glu Glu Asn Ile Lys Tyr Leu His Asn Leu Val
 225 230 235 240

gtc tat cat gcc agg gcg ctg gac ctc agc gag gag gtc aac aac ata 768
 Val Tyr His Ala Arg Ala Leu Asp Leu Ser Glu Glu Val Asn Asn Ile
 245 250 255

ttc agc ttc ctg atc ctg tgg aac ttt att gcc gca tcg ctc gtg att 816
 Phe Ser Phe Leu Ile Leu Trp Asn Phe Ile Ala Ala Ser Leu Val Ile
 260 265 270

tgc ttc gct ggc ttt cag att aca gcc tca aat gtg gag gac ata ggg 864
 Cys Phe Ala Gly Phe Gln Ile Thr Ala Ser Asn Val Glu Asp Ile Gly
 275 280 285

gtg tac ttc ata ttt ttt tca gct tcg ctg gtt caa gtc ttt aaa tgt 912
 Val Tyr Phe Ile Phe Phe Ser Ala Ser Leu Val Gln Val Phe Lys Cys
 290 295 300

tct ttt cag agc tct cgg att ggc cat tcg gca ttt aat cag aac tgg 960
 Ser Phe Gln Ser Ser Arg Ile Gly His Ser Ala Phe Asn Gln Asn Trp
 305 310 315 320

ttg cca tgc agc acc aaa tac aaa cgc atc ctg cag ttt att atc gcg 1008
 Leu Pro Cys Ser Thr Lys Tyr Lys Arg Ile Leu Gln Phe Ile Ile Ala
 325 330 335

cgc agc cag aag ccc gcc tct ata aga ccg cct acc ttt cca ccc ata 1056
 Arg Ser Gln Lys Pro Ala Ser Ile Arg Pro Pro Thr Phe Pro Pro Ile
 340 345 350

tct ttt aat acc ttt atg aag gta atc agc atg tcg tat cag ttt ttt 1104
 Ser Phe Asn Thr Phe Met Lys Val Ile Ser Met Ser Tyr Gln Phe Phe
 355 360 365

gca ctg ctc cgc acc aca tat tat ggt 1131
 Ala Leu Leu Arg Thr Thr Tyr Tyr Gly
 370 375

<210> 58
 <211> 377
 <212> PRT
 <213> Drosophila melanogaster

<400> 58

Met Thr Phe Tyr Lys Thr Ile Gly Glu Asp Leu Tyr Ser Asp Arg Asp
 1 5 10 15

Pro Asn Val Ile Arg Arg Tyr Leu Leu Arg Phe Tyr Leu Val Leu Gly
 20 25 30

Phe Leu Asn Phe Asn Ala Tyr Val Val Gly Glu Ile Ala Tyr Phe Ile
 35 40 45

Val His Ile Met Ser Thr Thr Thr Leu Leu Glu Ala Thr Ala Val Ala
 50 55 60

Pro Cys Ile Gly Phe Ser Phe Met Ala Asp Phe Lys Gln Phe Gly Leu
 65 70 75 80

Thr Val Asn Arg Lys Arg Leu Val Arg Leu Leu Asp Asp Leu Lys Glu
 85 90 95

Ile Phe Pro Leu Asp Leu Glu Ala Gln Arg Lys Tyr Asn Val Ser Phe
 100 105 110

Tyr Arg Lys His Met Asn Arg Val Met Thr Leu Phe Thr Ile Leu Cys
 115 120 125

Met Thr Tyr Thr Ser Ser Phe Ser Phe Tyr Pro Ala Ile Lys Ser Thr
 130 135 140

Ile Lys Tyr Tyr Leu Met Gly Ser Glu Ile Phe Glu Arg Asn Tyr Gly
 145 150 155 160

Phe His Ile Leu Phe Pro Tyr Asp Ala Glu Thr Asp Leu Thr Val Tyr
 165 170 175

Trp Phe Ser Tyr Trp Gly Leu Ala His Cys Ala Tyr Val Ala Gly Val
 180 185 190

Ser Tyr Val Cys Val Asp Leu Leu Leu Ile Ala Thr Ile Thr Gln Leu
 195 200 205

Thr Met His Phe Asn Phe Ile Ala Asn Asp Leu Glu Ala Tyr Glu Gly
 210 215 220

Gly Asp His Thr Asp Glu Glu Asn Ile Lys Tyr Leu His Asn Leu Val
 225 230 235 240

Val Tyr His Ala Arg Ala Leu Asp Leu Ser Glu Glu Val Asn Asn Ile
 245 250 255

Phe Ser Phe Leu Ile Leu Trp Asn Phe Ile Ala Ala Ser Leu Val Ile
 260 265 270

Cys Phe Ala Gly Phe Gln Ile Thr Ala Ser Asn Val Glu Asp Ile Gly
 275 280 285

Val Tyr Phe Ile Phe Phe Ser Ala Ser Leu Val Gln Val Phe Lys Cys
 290 295 300

Ser Phe Gln Ser Ser Arg Ile Gly His Ser Ala Phe Asn Gln Asn Trp
 305 310 315 320

Leu Pro Cys Ser Thr Lys Tyr Lys Arg Ile Leu Gln Phe Ile Ile Ala
 325 330 335

Arg Ser Gln Lys Pro Ala Ser Ile Arg Pro Pro Thr Phe Pro Pro Ile
 340 345 350

Ser Phe Asn Thr Phe Met Lys Val Ile Ser Met Ser Tyr Gln Phe Phe
 355 360 365

Ala Leu Leu Arg Thr Thr Tyr Tyr Gly
 370 375

<210> 59
 <211> 1161
 <212> DNA
 <213> Drosophila melanogaster

<220>
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 <222> (1)..(1161)
 <223> DOR 94D.1

<400> 59
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 Met Asp Lys His Lys Asp Arg Ile Glu Ser Met Arg Leu Ile Leu Gln
 1 5 10 15

gtc atg caa cta ttt ggc ctc tgg ccg tgg tcc ttg aaa tcg gaa gag 96

Val Met Gln Leu Phe Gly Leu Trp Pro Trp Ser Leu Lys Ser Glu Glu	
20 25 30	
gag tgg act ttc acc ggt ttt gta aag cgc aac tat cgc ttc ctg ctc	144
Glu Trp Thr Phe Thr Gly Phe Val Lys Arg Asn Tyr Arg Phe Leu Leu	
35 40 45	
cat ctg ccc att acc ttc acc ttt att gga ctc atg tgg ctg gag gcc	192
His Leu Pro Ile Thr Phe Thr Phe Ile Gly Leu Met Trp Leu Glu Ala	
50 55 60	
ttc atc tcg agc aat ctg gag cag gct ggc cag gtt ctg tac atg tcc	240
Phe Ile Ser Ser Asn Leu Glu Gln Ala Gly Gln Val Leu Tyr Met Ser	
65 70 75 80	
atc acc gag atg gct ttg gtg gtg aaa atc ctg agc att tgg cac tat	288
Ile Thr Glu Met Ala Leu Val Val Lys Ile Leu Ser Ile Trp His Tyr	
85 90 95	
cgc acc gaa gct tgg cgg ctg atg tac gaa ctc caa cat gct ccg gac	336
Arg Thr Glu Ala Trp Arg Leu Met Tyr Glu Leu Gln His Ala Pro Asp	
100 105 110	
tac caa ctc cac aac cag gag gag gta gac ttt tgg cgc cgg gag caa	384
Tyr Gln Leu His Asn Gln Glu Glu Val Asp Phe Trp Arg Arg Glu Gln	
115 120 125	
cga ttc ttc aag tgg ttc ttc tac atc tac att ctg att agc ttg ggc	432
Arg Phe Phe Lys Trp Phe Phe Tyr Ile Tyr Ile Leu Ile Ser Leu Gly	
130 135 140	
gtg gta tat agt ggc tgc act gga gta ctt ttt ctg gag ggc tac gaa	480
Val Val Tyr Ser Gly Cys Thr Gly Val Leu Phe Leu Glu Gly Tyr Glu	
145 150 155 160	
ctg ccc ttt gcc tac tac gtg ccc ttc gaa tgg cag aac gag aga agg	528
Leu Pro Phe Ala Tyr Tyr Val Pro Phe Glu Trp Gln Asn Glu Arg Arg	
165 170 175	
tac tgg ttc gcc tat ggt tac gat atg gcg ggc atg acg ctg acc tgc	576
Tyr Trp Phe Ala Tyr Gly Tyr Asp Met Ala Gly Met Thr Leu Thr Cys	
180 185 190	
atc tca aac att acc ctg gac acc ctg ggt tgc tat ttc ctg ttc cat	624
Ile Ser Asn Ile Thr Leu Asp Thr Leu Gly Cys Tyr Phe Leu Phe His	
195 200 205	
atc tct ctt ttg tac cga ctg ctt ggt ctg cga ttg agg gaa acg aag	672

Ile Ser Leu Leu Tyr Arg Leu Leu Gly Leu Arg Leu Arg Glu Thr Lys	
210	215 220
aat atg aag aat gat acc att ttt ggc cag cag ttg cgt gcc atc ttc	720
Asn Met Lys Asn Asp Thr Ile Phe Gly Gln Gln Leu Arg Ala Ile Phe	
225 230 235 240	
att atg cat cag agg att aga agc cta acc ctg acc tgc cag aga atc	768
Ile Met His Gln Arg Ile Arg Ser Leu Thr Leu Thr Cys Gln Arg Ile	
245 250 255	
gta tct ccc tat atc cta tct cag atc att ttg agt gcc ctg atc atc	816
Val Ser Pro Tyr Ile Leu Ser Gln Ile Ile Leu Ser Ala Leu Ile Ile	
260 265 270	
tgc ttt agt gga tac cgc ttg cag cat gtg gga att cgc gat aat ccc	864
Cys Phe Ser Gly Tyr Arg Leu Gln His Val Gly Ile Arg Asp Asn Pro	
275 280 285	
ggc cag ttt ata tcc atg ttg cag ttt gtc agt gtg atg atc ctg cag	912
Gly Gln Phe Ile Ser Met Leu Gln Phe Val Ser Val Met Ile Leu Gln	
290 295 300	
att tac ttg ccc tgc tac tat gga aac gag ata acc gtg tat gcc aat	960
Ile Tyr Leu Pro Cys Tyr Tyr Gly Asn Glu Ile Thr Val Tyr Ala Asn	
305 310 315 320	
cag ctg acc aac gag gtt tac cat acc aat tgg ctg gaa tgt cgg cca	1008
Gln Leu Thr Asn Glu Val Tyr His Thr Asn Trp Leu Glu Cys Arg Pro	
325 330 335	
ccg att cga aag tta ctc aat gcc tac atg gag cac ctg aag aaa ccg	1056
Pro Ile Arg Lys Leu Leu Asn Ala Tyr Met Glu His Leu Lys Lys Pro	
340 345 350	
gtg acc atc cgg gct ggc aac tac ttc gcc gtg gga cta cca att ttt	1104
Val Thr Ile Arg Ala Gly Asn Tyr Phe Ala Val Gly Leu Pro Ile Phe	
355 360 365	
gtt aag acc atc aac aac gcc tac agt ttc ttg gct tta tta cta aat	1152
Val Lys Thr Ile Asn Asn Ala Tyr Ser Phe Leu Ala Leu Leu Leu Asn	
370 375 380	
gta tcg aat	1161
Val Ser Asn	
385	

<210> 60
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 <212> PRT
 <213> Drosophila melanogaster

<400> 60

Met Asp Lys His Lys Asp Arg Ile Glu Ser Met Arg Leu Ile Leu Gln
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Val Met Gln Leu Phe Gly Leu Trp Pro Trp Ser Leu Lys Ser Glu Glu
 20 25 30

Glu Trp Thr Phe Thr Gly Phe Val Lys Arg Asn Tyr Arg Phe Leu Leu
 35 40 45

His Leu Pro Ile Thr Phe Thr Phe Ile Gly Leu Met Trp Leu Glu Ala
 50 55 60

Phe Ile Ser Ser Asn Leu Glu Gln Ala Gly Gln Val Leu Tyr Met Ser
 65 70 75 80

Ile Thr Glu Met Ala Leu Val Val Lys Ile Leu Ser Ile Trp His Tyr
 85 90 95

Arg Thr Glu Ala Trp Arg Leu Met Tyr Glu Leu Gln His Ala Pro Asp
 100 105 110

Tyr Gln Leu His Asn Gln Glu Glu Val Asp Phe Trp Arg Arg Glu Gln
 115 120 125

Arg Phe Phe Lys Trp Phe Phe Tyr Ile Tyr Ile Leu Ile Ser Leu Gly
 130 135 140

Val Val Tyr Ser Gly Cys Thr Gly Val Leu Phe Leu Glu Gly Tyr Glu
 145 150 155 160

Leu Pro Phe Ala Tyr Tyr Val Pro Phe Glu Trp Gln Asn Glu Arg Arg
 165 170 175

Tyr Trp Phe Ala Tyr Gly Tyr Asp Met Ala Gly Met Thr Leu Thr Cys
 180 185 190

Ile Ser Asn Ile Thr Leu Asp Thr Leu Gly Cys Tyr Phe Leu Phe His
 195 200 205

Ile Ser Leu Leu Tyr Arg Leu Leu Gly Leu Arg Leu Arg Glu Thr Lys
 210 215 220

003240 254660

Asn Met Lys Asn Asp Thr Ile Phe Gly Gln Gln Leu Arg Ala Ile Phe
225 230 235 240

Ile Met His Gln Arg Ile Arg Ser Leu Thr Leu Thr Cys Gln Arg Ile
245 250 255

Val Ser Pro Tyr Ile Leu Ser Gln Ile Ile Leu Ser Ala Leu Ile Ile
260 265 270

Cys Phe Ser Gly Tyr Arg Leu Gln His Val Gly Ile Arg Asp Asn Pro
275 280 285

Gly Gln Phe Ile Ser Met Leu Gln Phe Val Ser Val Met Ile Leu Gln
290 295 300

Ile Tyr Leu Pro Cys Tyr Tyr Gly Asn Glu Ile Thr Val Tyr Ala Asn
305 310 315 320

Gln Leu Thr Asn Glu Val Tyr His Thr Asn Trp Leu Glu Cys Arg Pro
325 330 335

Pro Ile Arg Lys Leu Leu Asn Ala Tyr Met Glu His Leu Lys Lys Pro
340 345 350

Val Thr Ile Arg Ala Gly Asn Tyr Phe Ala Val Gly Leu Pro Ile Phe
355 360 365

Val Lys Thr Ile Asn Asn Ala Tyr Ser Phe Leu Ala Leu Leu Leu Asn
370 375 380

Val Ser Asn
385

<210> 61
<211> 1101
<212> DNA
<213> Drosophila melanogaster

<220>
<221> CDS
<222> (1)..(1101)

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atg gag tct aca aat cgc cta agt gcc atc caa aca ctt tta gta atc 48
Met Glu Ser Thr Asn Arg Leu Ser Ala Ile Gln Thr Leu Leu Val Ile
1 5 10 15

caa cgt tgg ata gga ctt ctt aaa tgg gaa aac gag ggc gag gat gga Gln Arg Trp Ile Gly Leu Leu Lys Trp Glu Asn Glu Gly Glu Asp Gly	96
20 25 30	
gta tta acc tgg cta aaa cga ata tat cct ttt gta ctg cac ctt cca Val Leu Thr Trp Leu Lys Arg Ile Tyr Pro Phe Val Leu His Leu Pro	144
35 40 45	
ctg acc ttc acg tat att gcc tta atg tgg tat gaa gct att aca tcg Leu Thr Phe Thr Tyr Ile Ala Leu Met Trp Tyr Glu Ala Ile Thr Ser	192
50 55 60	
tca gat ttt gag gaa gct ggt caa gtt ctg tac atg tcc atc acc gaa Ser Asp Phe Glu Glu Ala Gly Gln Val Leu Tyr Met Ser Ile Thr Glu	240
65 70 75 80	
ctg gca ttg gtc act aaa ctg ctg aat att tgg tat cgt cgt cat gaa Leu Ala Leu Val Thr Lys Leu Leu Asn Ile Trp Tyr Arg Arg His Glu	288
85 90 95	
gct gct agt cta atc cac gaa ttg caa cac gat ccc gca ttt aat ctg Ala Ala Ser Leu Ile His Glu Leu Gln His Asp Pro Ala Phe Asn Leu	336
100 105 110	
cgc aat tcg gag gaa atc aaa ttc tgg cag caa aat cag agg aac ttt Arg Asn Ser Glu Glu Ile Lys Phe Trp Gln Gln Asn Gln Arg Asn Phe	384
115 120 125	
aag aga ata ttt tac tgg tac atc tgg ggc agc ctt ttc gtg gct gta Lys Arg Ile Phe Tyr Trp Tyr Ile Trp Gly Ser Leu Phe Val Ala Val	432
130 135 140	
atg ggt tat ata agc gtg ttt ttc cag gag gat tac gag ctg ccc ttt Met Gly Tyr Ile Ser Val Phe Phe Gln Glu Asp Tyr Glu Leu Pro Phe	480
145 150 155 160	
ggc tac tac gtg cca ttc gag tgg cgc acc agg gaa cga tac ttc tac Gly Tyr Tyr Val Pro Phe Glu Trp Arg Thr Arg Glu Arg Tyr Phe Tyr	528
165 170 175	
gct tgg ggc tat aat gtg gtg gcc atg acc ctg tgc tgt cta tcc aac Ala Trp Gly Tyr Asn Val Val Ala Met Thr Leu Cys Cys Leu Ser Asn	576
180 185 190	
atc cta ctg gac aca cta ggc tgt tat ttc atg ttc cac atc gcc tcg Ile Leu Leu Asp Thr Leu Gly Cys Tyr Phe Met Phe His Ile Ala Ser	624
195 200 205	

ctt ttc agg ctt ttg gga atg cga ctg gag gcc ttg aaa aat gca gcc 672
 Leu Phe Arg Leu Leu Gly Met Arg Leu Glu Ala Leu Lys Asn Ala Ala
 210 215 220

 gaa gag aaa gcc aga ccg gag ttg cgc cgc att ttc caa ctg cac act 720
 Glu Glu Lys Ala Arg Pro Glu Leu Arg Arg Ile Phe Gln Leu His Thr
 225 230 235 240

 aaa gtc cgc cga ttg acg agg gaa tgc gaa gtg tta gtt tca ccc tat 768
 Lys Val Arg Arg Leu Thr Arg Glu Cys Glu Val Leu Val Ser Pro Tyr
 245 250 255

 gtt cta tcc caa gtg gtc ttc agt gcc ttc atc atc tgc ttc agt gcc 816
 Val Leu Ser Gln Val Val Phe Ser Ala Phe Ile Ile Cys Phe Ser Ala
 260 265 270

 tat cga ctg gtg cac atg ggc ttc aag cag cga cct gga ctc ttc gtg 864
 Tyr Arg Leu Val His Met Gly Phe Lys Gln Arg Pro Gly Leu Phe Val
 275 280 285

 acc acc gtg caa ttc gtg gcc gtc atg atc gtc cag att ttc ttg ccc 912
 Thr Thr Val Gln Phe Val Ala Val Met Ile Val Gln Ile Phe Leu Pro
 290 295 300

 tgt tac tac ggc aat gag ttg acc ttt cat gcc aat gca ctc act aat 960
 Cys Tyr Tyr Gly Asn Glu Leu Thr Phe His Ala Asn Ala Leu Thr Asn
 305 310 315 320

 agt gtc ttc ggt acc aat tgg ctg gag tac tcc gtg ggc act cgc aag 1008
 Ser Val Phe Gly Thr Asn Trp Leu Glu Tyr Ser Val Gly Thr Arg Lys
 325 330 335

 ctg ctt aac tgc tac atg gag ttc ctc aag cga ccg gtt aaa acc atc 1056
 Leu Leu Asn Cys Tyr Met Glu Phe Leu Lys Arg Pro Val Lys Thr Ile
 340 345 350

 aac aat gcc tac agt ttc ttc gcc ctg ctg cta aag ata tcc aag 1101
 Asn Asn Ala Tyr Ser Phe Phe Ala Leu Leu Leu Lys Ile Ser Lys
 355 360 365

<210> 62
 <211> 367
 <212> PRT
 <213> Drosophila melanogaster

 <400> 62

Val Leu Ser Gln Val Val Phe Ser Ala Phe Ile Ile Cys Phe Ser Ala
260 265 270

Tyr Arg Leu Val His Met Gly Phe Lys Gln Arg Pro Gly Leu Phe Val
275 280 285

Thr Thr Val Gln Phe Val Ala Val Met Ile Val Gln Ile Phe Leu Pro
290 295 300

Cys Tyr Tyr Gly Asn Glu Leu Thr Phe His Ala Asn Ala Leu Thr Asn
305 310 315 320

Ser Val Phe Gly Thr Asn Trp Leu Glu Tyr Ser Val Gly Thr Arg Lys
325 330 335

Leu Leu Asn Cys Tyr Met Glu Phe Leu Lys Arg Pro Val Lys Thr Ile
340 345 350

Asn Asn Ala Tyr Ser Phe Phe Ala Leu Leu Leu Lys Ile Ser Lys
355 360 365

<210> 63

<211> 1095

<212> DNA

<213> Drosophila melanogaster

<220>

<221> CDS

<222> (1)..(1095)

<223> DORLU 1.1

<400> 63

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Met Trp Leu Ile Gly Trp Ile Pro Pro Lys Glu Gly Val Leu Arg Tyr
1 5 10 15

gtg tat ctc ttc tgg acc tgc gtg ccc ttc gcc ttc ggg gtg ttt tac 96
Val Tyr Leu Phe Trp Thr Cys Val Pro Phe Ala Phe Gly Val Phe Tyr
20 25 30

ctg ccc gtg ggc ttc atc atc agc tac gtg cag gag ttc aag aac ttc 144
Leu Pro Val Gly Phe Ile Ile Ser Tyr Val Gln Glu Phe Lys Asn Phe
35 40 45

acg ccg ggc gag ttc ctt acc tcg ctg cag gtg tgc atc aat gtg tat 192
Thr Pro Gly Glu Phe Leu Thr Ser Leu Gln Val Cys Ile Asn Val Tyr

60

acc atc ttc gtg caa ttc gcg ctg att ggt tcc gtt ttg ggc ctg acc 768
Thr Ile Phe Val Gln Phe Ala Leu Ile Gly Ser Val Leu Gly Leu Thr

Val Leu Phe Met His His Val Gln Gln Pro Ile Ile Phe Ile Ala Gly
 325 330 335

Gly Ile Phe Pro Ile Ser Met Asn Ser Asn Ile Thr Val Arg Ile Thr
 340 345 350

Ser Phe Leu Pro Thr Ala Tyr Phe Thr Phe Asp Pro Phe
 355 360 365

<210> 65
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 <212> DNA
 <213> Drosophila melanogaster

<220>
 <221> CDS
 <222> (1)..(1233)
 <223> DORLU 2.1

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 Met Thr Lys Phe Phe Phe Lys Arg Leu Gln Thr Ala Pro Leu Asp Gln
 1 5 10 15
 gag gtg agt tcc ctt gat gcc agc gac tac tac tac cgc atc gca ttt 96
 Glu Val Ser Ser Leu Asp Ala Ser Asp Tyr Tyr Tyr Arg Ile Ala Phe
 20 25 30
 ttc ctg ggc tgg acc ccg ccc aag ggg gct ctg ctc cga tgg atc tac 144
 Phe Leu Gly Trp Thr Pro Pro Lys Gly Ala Leu Leu Arg Trp Ile Tyr
 35 40 45
 tcc ctg tgg act ctg acc acg atg tgg ctg ggt atc gtg tac ctg ccg 192
 Ser Leu Trp Thr Leu Thr Thr Met Trp Leu Gly Ile Val Tyr Leu Pro
 50 55 60
 ctc gga ctg agc ctc acc tat gtg aag cac ttc gat aga ttc acg ccg 240
 Leu Gly Leu Ser Leu Thr Tyr Val Lys His Phe Asp Arg Phe Thr Pro
 65 70 75 80
 acg gag ttc ctg acc tcc ctg cag gtg gat atc aac tgc atc ggg aac 288
 Thr Glu Phe Leu Thr Ser Leu Gln Val Asp Ile Asn Cys Ile Gly Asn
 85 90 95
 gtg atc aag tca tgc gta act tat tcc cag atg tgg cgt ttt cgc cgg 336

Val Ile Lys Ser Cys Val Thr Tyr Ser Gln Met Trp Arg Phe Arg Arg	
100	110
atg aat gag ctt atc tcg tcc ctg gac aag aga tgt gtg act acg aca	384
Met Asn Glu Leu Ile Ser Ser Leu Asp Lys Arg Cys Val Thr Thr Thr	
115	125
cag cgt cga att ttc cat aag atg gtg gca cgg gtt aat ctc atc gtg	432
Gln Arg Arg Ile Phe His Lys Met Val Ala Arg Val Asn Leu Ile Val	
130	140
att ctg ttc ttg tcc acg tac ttg ggc ttc tgc ttt cta act ctg ttc	480
Ile Leu Phe Leu Ser Thr Tyr Leu Gly Phe Cys Phe Leu Thr Leu Phe	
145	160
act tcg gtt ttc gct ggc aaa gct cct tgg cag ctg tac aac cca ctg	528
Thr Ser Val Phe Ala Gly Lys Ala Pro Trp Gln Leu Tyr Asn Pro Leu	
165	175
gtg gac tgg cgg aaa ggc cat tgg cag cta tgg att gcc tcc atc ctg	576
Val Asp Trp Arg Lys Gly His Trp Gln Leu Trp Ile Ala Ser Ile Leu	
180	190
gag tac tgt gtg gtc tcc att ggc acc atg cag gag ttg atg tcc gac	624
Glu Tyr Cys Val Val Ser Ile Gly Thr Met Gln Glu Leu Met Ser Asp	
195	205
acc tac gcc ata gtg ttc atc tcc ttg ttc cgc tgc cac ctg gct att	672
Thr Tyr Ala Ile Val Phe Ile Ser Leu Phe Arg Cys His Leu Ala Ile	
210	220
ctc aga gat cgc ata gct aat ctg cgg cag gat ccg aaa ctc agt gag	720
Leu Arg Asp Arg Ile Ala Asn Leu Arg Gln Asp Pro Lys Leu Ser Glu	
225	240
atg gaa cac tat gag cag atg gtg gcc tgc att cag gat cat cga acc	768
Met Glu His Tyr Glu Gln Met Val Ala Cys Ile Gln Asp His Arg Thr	
245	255
atc ata cag tgc tcc cag att att cga ccc atc ctg tcg atc act atc	816
Ile Ile Gln Cys Ser Gln Ile Ile Arg Pro Ile Leu Ser Ile Thr Ile	
260	270
ttt gcc cag ttc atg ctg gtt ggc att gac ttg ggt ctg gcg gcc atc	864
Phe Ala Gln Phe Met Leu Val Gly Ile Asp Leu Gly Leu Ala Ala Ile	
275	285
agc atc ctc ttc ttt ccg aac acc att tgg acg atc atg gca aac gtg	912

50	55	60
Leu Gly Leu Ser Leu Thr Tyr Val Lys His Phe Asp Arg Phe Thr Pro		
65	70	75 80
Thr Glu Phe Leu Thr Ser Leu Gln Val Asp Ile Asn Cys Ile Gly Asn		
	85	90 95
Val Ile Lys Ser Cys Val Thr Tyr Ser Gln Met Trp Arg Phe Arg Arg		
	100	105 110
Met Asn Glu Leu Ile Ser Ser Leu Asp Lys Arg Cys Val Thr Thr Thr		
	115	120 125
Gln Arg Arg Ile Phe His Lys Met Val Ala Arg Val Asn Leu Ile Val		
	130	135 140
Ile Leu Phe Leu Ser Thr Tyr Leu Gly Phe Cys Phe Leu Thr Leu Phe		
	145	150 155 160
Thr Ser Val Phe Ala Gly Lys Ala Pro Trp Gln Leu Tyr Asn Pro Leu		
	165	170 175
Val Asp Trp Arg Lys Gly His Trp Gln Leu Trp Ile Ala Ser Ile Leu		
	180	185 190
Glu Tyr Cys Val Val Ser Ile Gly Thr Met Gln Glu Leu Met Ser Asp		
	195	200 205
Thr Tyr Ala Ile Val Phe Ile Ser Leu Phe Arg Cys His Leu Ala Ile		
	210	215 220
Leu Arg Asp Arg Ile Ala Asn Leu Arg Gln Asp Pro Lys Leu Ser Glu		
	225	230 235 240
Met Glu His Tyr Glu Gln Met Val Ala Cys Ile Gln Asp His Arg Thr		
	245	250 255
Ile Ile Gln Cys Ser Gln Ile Ile Arg Pro Ile Leu Ser Ile Thr Ile		
	260	265 270
Phe Ala Gln Phe Met Leu Val Gly Ile Asp Leu Gly Leu Ala Ala Ile		
	275	280 285
Ser Ile Leu Phe Phe Pro Asn Thr Ile Trp Thr Ile Met Ala Asn Val		
	290	295 300
Ser Phe Ile Val Ala Ile Cys Thr Glu Ser Phe Pro Cys Cys Met Leu		

305 310 315 320
 Cys Glu His Leu Ile Glu Asp Ser Val His Val Ser Asn Ala Leu Phe
 325 330 335
 His Ser Asn Trp Ile Thr Ala Asp Arg Ser Tyr Lys Ser Ala Val Leu
 340 345 350
 Tyr Phe Leu His Arg Ala Gln Gln Pro Ile Gln Phe Thr Ala Gly Ser
 355 360 365
 Ile Phe Pro Ile Ser Val Gln Ser Asn Ile Ala Val Ala Lys Phe Ala
 370 375 380
 Phe Thr Ile Ile Thr Ile Val Asn Gln Met Asn Leu Gly Glu Lys Phe
 385 390 395 400
 Phe Ser Asp Arg Ser Asn Gly Asp Ile Asn Pro
 405 410

<210> 67
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 <212> DNA
 <213> Drosophila melanogaster

<220>
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 <222> (1)..(1191)
 <223> DORLU 4.1

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 Met Ile Phe Lys Tyr Ile Gln Glu Pro Val Leu Gly Ser Leu Phe Arg
 1 5 10 15
 tcc cgg gat tcg ctg atc tac tta aac aga tcc ata gat caa atg gga 96
 Ser Arg Asp Ser Leu Ile Tyr Leu Asn Arg Ser Ile Asp Gln Met Gly
 20 25 30
 tgg aga ctg ccg cca cga act aag ccg tac tgg tgg ctc tat tac att 144
 Trp Arg Leu Pro Pro Arg Thr Lys Pro Tyr Trp Trp Leu Tyr Tyr Ile
 35 40 45
 tgg aca ttg gtg gtc ata gta ctc gtc ttt atc ttt ata ccc tat gga 192
 Trp Thr Leu Val Val Ile Val Leu Val Phe Ile Phe Ile Pro Tyr Gly
 50 55 60

aac act ctg cgt ccc atg ata tcc gcc acg atg ttc atc caa cta cta 816
 Asn Thr Leu Arg Pro Met Ile Ser Ala Thr Met Phe Ile Gln Leu Leu
 260 265 270

tcc gtt ggc tta ctt ttg ggt ctg gca gcg gtg tcc atg cag ttc tat 864
 Ser Val Gly Leu Leu Leu Gly Leu Ala Ala Val Ser Met Gln Phe Tyr
 275 280 285

aac acc gta atg gag cgt gtt gtc tcc ggg gtc tac acc ata gcc att 912
 Asn Thr Val Met Glu Arg Val Val Ser Gly Val Tyr Thr Ile Ala Ile
 290 295 300

cta tcc cag acc ttt cca ttt tgc tat gtc tgt gag cag ctg agc agc 960
 Leu Ser Gln Thr Phe Pro Phe Cys Tyr Val Cys Glu Gln Leu Ser Ser
 305 310 315 320

gat tgc gaa tcc ctg acc aac aca ctg ttc cat tcc aag tgg att gga 1008
 Asp Cys Glu Ser Leu Thr Asn Thr Leu Phe His Ser Lys Trp Ile Gly
 325 330 335

gct gag cga cga tac aga acc acg atg ttg tac ttc att cac aat gtt 1056
 Ala Glu Arg Arg Tyr Arg Thr Thr Met Leu Tyr Phe Ile His Asn Val
 340 345 350

cag cag tcg att ttg ttc act gcg ggc gga att ttc ccc ata tgt cta 1104
 Gln Gln Ser Ile Leu Phe Thr Ala Gly Gly Ile Phe Pro Ile Cys Leu
 355 360 365

aac acc aat ata aag atg gcc aag ttc gct ttc tca gtg gtg acc att 1152
 Asn Thr Asn Ile Lys Met Ala Lys Phe Ala Phe Ser Val Val Thr Ile
 370 375 380

gta aat gag atg gac ttg gcc gag aaa ttg aga agg gag 1191
 Val Asn Glu Met Asp Leu Ala Glu Lys Leu Arg Arg Glu
 385 390 395

<210> 68

<211> 397

<212> PRT

<213> Drosophila melanogaster

<400> 68

Met Ile Phe Lys Tyr Ile Gln Glu Pro Val Leu Gly Ser Leu Phe Arg
 1 5 10 15

Ser Arg Asp Ser Leu Ile Tyr Leu Asn Arg Ser Ile Asp Gln Met Gly

00543457 013500

20	25	30
Trp Arg Leu Pro Pro Arg Thr Lys Pro Tyr Trp Trp Leu Tyr Tyr Ile		
35	40	45
Trp Thr Leu Val Val Ile Val Leu Val Phe Ile Phe Ile Pro Tyr Gly		
50	55	60
Leu Ile Met Thr Gly Ile Lys Glu Phe Lys Asn Phe Thr Thr Thr Asp		
65	70	75
Leu Phe Thr Tyr Val Gln Val Pro Val Asn Thr Asn Ala Ser Ile Met		
85	90	95
Lys Gly Ile Ile Val Leu Phe Met Arg Arg Arg Phe Ser Arg Ala Gln		
100	105	110
Lys Met Met Asp Ala Met Asp Ile Arg Cys Thr Lys Met Glu Glu Lys		
115	120	125
Val Gln Val His Arg Ala Ala Ala Leu Cys Asn Arg Val Val Val Ile		
130	135	140
Tyr His Cys Ile Tyr Phe Gly Tyr Leu Ser Met Ala Leu Thr Gly Ala		
145	150	155
Leu Val Ile Gly Lys Thr Pro Phe Cys Leu Tyr Asn Pro Leu Val Asn		
165	170	175
Pro Asp Asp His Phe Tyr Leu Ala Thr Ala Ile Glu Ser Val Thr Met		
180	185	190
Ala Gly Ile Ile Leu Ala Asn Leu Ile Leu Asp Val Tyr Pro Ile Ile		
195	200	205
Tyr Val Val Val Leu Arg Ile His Met Glu Leu Leu Ser Glu Arg Ile		
210	215	220
Lys Thr Leu Arg Thr Asp Val Glu Lys Gly Asp Asp Gln His Tyr Ala		
225	230	235
Glu Leu Val Glu Cys Val Lys Asp His Lys Leu Ile Val Glu Tyr Gly		
245	250	255
Asn Thr Leu Arg Pro Met Ile Ser Ala Thr Met Phe Ile Gln Leu Leu		
260	265	270
Ser Val Gly Leu Leu Leu Gly Leu Ala Ala Val Ser Met Gln Phe Tyr		

gat ttg att aag tgc atc aag gat cac aat ctc att att gac tat gct	768
Asp Leu Ile Lys Cys Ile Lys Asp His Asn Leu Ile Ile Asp Tyr Ala	
245 250 255	
gca gca ata cga cca gcg gtt acc cgc aca att ttc gtt caa ttc ctc	816
Ala Ala Ile Arg Pro Ala Val Thr Arg Thr Ile Phe Val Gln Phe Leu	
260 265 270	
ttg atc gga att tgc ctt ggc ctt tca atg atc aat cta ctc ttc ttt	864
Leu Ile Gly Ile Cys Leu Gly Leu Ser Met Ile Asn Leu Leu Phe Phe	
275 280 285	
gcc gac atc tgg aca gga ttg gcc aca gtg gct tac atc aat ggt cta	912
Ala Asp Ile Trp Thr Gly Leu Ala Thr Val Ala Tyr Ile Asn Gly Leu	
290 295 300	
atg gtg cag aca ttt cca ttt tgc ttc gtt tgt gat cta ctc aaa aag	960
Met Val Gln Thr Phe Pro Phe Cys Phe Val Cys Asp Leu Leu Lys Lys	
305 310 315 320	
gat tgt gaa ctt ctt gtg tcg gcc ata ttt cat tcc aac tgg att aat	1008
Asp Cys Glu Leu Leu Val Ser Ala Ile Phe His Ser Asn Trp Ile Asn	
325 330 335	
tca agc cgc agt tac aag tca tct ttg aga tat ttt ctg aag aac gcc	1056
Ser Ser Arg Ser Tyr Lys Ser Ser Leu Arg Tyr Phe Leu Lys Asn Ala	
340 345 350	
cag aaa tca att gct ttt aca gcc ggc tct att ttt ccc att tct act	1104
Gln Lys Ser Ile Ala Phe Thr Ala Gly Ser Ile Phe Pro Ile Ser Thr	
355 360 365	
ggc tcg aat att aag gtg gct aag ctg gca ttt tcg gtg gtt act ttt	1152
Gly Ser Asn Ile Lys Val Ala Lys Leu Ala Phe Ser Val Val Thr Phe	
370 375 380	
gtc aat caa ctt aac ata gct gac aga ttg aca aag aac	1191
Val Asn Gln Leu Asn Ile Ala Asp Arg Leu Thr Lys Asn	
385 390 395	

<210> 70

<211> 397

<212> PRT

<213> Drosophila melanogaster

<400> 70

Met Leu Phe Asn Tyr Leu Arg Lys Pro Asn Pro Thr Asn Leu Leu Thr

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Ser Pro Asp Ser Phe Arg Tyr Phe Glu Tyr Gly Met Phe Cys Met Gly	20	25	30
Trp His Thr Pro Ala Thr His Lys Ile Ile Tyr Tyr Ile Thr Ser Cys	35	40	45
Leu Ile Phe Ala Trp Cys Ala Val Tyr Leu Pro Ile Gly Ile Ile Ile	50	55	60
Ser Phe Lys Thr Asp Ile Asn Thr Phe Thr Pro Asn Glu Leu Leu Thr	65	70	75
Val Met Gln Leu Phe Phe Asn Ser Val Gly Met Pro Phe Lys Val Leu	85	90	95
Phe Phe Asn Leu Tyr Ile Ser Gly Phe Tyr Lys Ala Lys Lys Leu Leu	100	105	110
Ser Glu Met Asp Lys Arg Cys Thr Thr Leu Lys Glu Arg Val Glu Val	115	120	125
His Gln Gly Val Val Arg Cys Asn Lys Ala Tyr Leu Ile Tyr Gln Phe	130	135	140
Ile Tyr Thr Ala Tyr Thr Ile Ser Thr Phe Leu Ser Ala Ala Leu Ser	145	150	155
Gly Lys Leu Pro Trp Arg Ile Tyr Asn Pro Phe Val Asp Phe Arg Glu	165	170	175
Ser Arg Ser Ser Phe Trp Lys Ala Ala Leu Asn Glu Thr Ala Leu Met	180	185	190
Leu Phe Ala Val Thr Gln Thr Leu Met Ser Asp Ile Tyr Pro Leu Leu	195	200	205
Tyr Gly Leu Ile Leu Arg Val His Leu Lys Leu Leu Arg Leu Arg Val	210	215	220
Glu Ser Leu Cys Thr Asp Ser Gly Lys Ser Asp Ala Glu Asn Glu Gln	225	230	235
Asp Leu Ile Lys Cys Ile Lys Asp His Asn Leu Ile Ile Asp Tyr Ala	245	250	255
Ala Ala Ile Arg Pro Ala Val Thr Arg Thr Ile Phe Val Gln Phe Leu			

260	265	270
Leu Ile Gly Ile Cys Leu Gly Leu Ser Met Ile Asn Leu Leu Phe Phe		
275	280	285
Ala Asp Ile Trp Thr Gly Leu Ala Thr Val Ala Tyr Ile Asn Gly Leu		
290	295	300
Met Val Gln Thr Phe Pro Phe Cys Phe Val Cys Asp Leu Leu Lys Lys		
305	310	315
Asp Cys Glu Leu Leu Val Ser Ala Ile Phe His Ser Asn Trp Ile Asn		
	325	330
		335
Ser Ser Arg Ser Tyr Lys Ser Ser Leu Arg Tyr Phe Leu Lys Asn Ala		
	340	345
		350
Gln Lys Ser Ile Ala Phe Thr Ala Gly Ser Ile Phe Pro Ile Ser Thr		
	355	360
		365
Gly Ser Asn Ile Lys Val Ala Lys Leu Ala Phe Ser Val Val Thr Phe		
	370	375
		380
Val Asn Gln Leu Asn Ile Ala Asp Arg Leu Thr Lys Asn		
385	390	395

<210> 71
 <211> 1239
 <212> DNA
 <213> Drosophila melanogaster

<220>
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 <223> DORLU 6.1

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Met Ala Val Ser Thr Arg Val Ala Thr Lys Gln Glu Val Pro Glu Ser	
1 5 10 15	
cgg cga gcg ttt agg aat ctc ttc aat tgc ttc tat gcc ctt ggc atg	96
Arg Arg Ala Phe Arg Asn Leu Phe Asn Cys Phe Tyr Ala Leu Gly Met	
20 25 30	
cag gca ccg gat ggc agt cga ccg acc acg agc agc aca tgg caa cgc	144

Gln	Ala	Pro	Asp	Gly	Ser	Arg	Pro	Thr	Thr	Ser	Ser	Thr	Trp	Gln	Arg		
		35					40					45					
atc	tac	gcc	tgc	ttc	tcg	gtg	gtc	atg	tac	gtg	tgg	caa	ctg	ctg	ctg	192	
Ile	Tyr	Ala	Cys	Phe	Ser	Val	Val	Met	Tyr	Val	Trp	Gln	Leu	Leu	Leu		
	50					55					60						
gtg	ccc	aca	ttc	ttt	gtg	atc	agc	tat	cgg	tac	atg	ggc	ggc	atg	gag	240	
Val	Pro	Thr	Phe	Phe	Val	Ile	Ser	Tyr	Arg	Tyr	Met	Gly	Gly	Met	Glu		
	65				70				75						80		
att	acc	cag	gtg	ctg	acc	tcc	gcc	cag	gtg	gcc	atc	gat	gcg	gtc	att	288	
Ile	Thr	Gln	Val	Leu	Thr	Ser	Ala	Gln	Val	Ala	Ile	Asp	Ala	Val	Ile		
			85					90						95			
ctg	ccg	gcc	aag	att	gtg	gca	ctg	gcg	tgg	aat	ttg	cca	ttg	ctg	cgc	336	
Leu	Pro	Ala	Lys	Ile	Val	Ala	Leu	Ala	Trp	Asn	Leu	Pro	Leu	Leu	Arg		
		100					105					110					
aga	gca	gag	cat	cat	ctg	gcc	gcc	ttg	gat	gcg	cgg	tgc	agg	gaa	cag	384	
Arg	Ala	Glu	His	His	Leu	Ala	Ala	Leu	Asp	Ala	Arg	Cys	Arg	Glu	Gln		
	115					120						125					
gag	gag	ttc	caa	ttg	atc	ctc	gat	gcg	gtg	agg	ttt	tgc	aac	tat	ctg	432	
Glu	Glu	Phe	Gln	Leu	Ile	Leu	Asp	Ala	Val	Arg	Phe	Cys	Asn	Tyr	Leu		
	130					135					140						
gta	tgg	ttc	tac	cag	atc	tgc	tat	gcc	atc	tac	tcc	tcg	tcg	aca	ttt	480	
Val	Trp	Phe	Tyr	Gln	Ile	Cys	Tyr	Ala	Ile	Tyr	Ser	Ser	Ser	Thr	Phe		
	145				150					155					160		
gtg	tgc	gcc	ttc	ctg	ctg	ggc	caa	ccg	cca	tat	gcc	ctc	tat	ttg	cct	528	
Val	Cys	Ala	Phe	Leu	Leu	Gly	Gln	Pro	Tyr	Ala	Leu	Tyr	Leu	Pro			
			165					170					175				
ggc	ctc	gat	tgg	cag	cgt	tcc	cag	atg	cag	ttc	tgc	atc	cag	gcc	tgg	576	
Gly	Leu	Asp	Trp	Gln	Arg	Ser	Gln	Met	Gln	Phe	Cys	Ile	Gln	Ala	Trp		
			180					185					190				
att	gag	ttc	ctt	atc	atg	aac	tgg	acg	tgc	ctg	cac	caa	gct	agc	gat	624	
Ile	Glu	Phe	Leu	Ile	Met	Asn	Trp	Thr	Cys	Leu	His	Gln	Ala	Ser	Asp		
	195					200						205					
gat	gtg	tac	gcc	gtt	atc	tat	ctg	tat	gtg	gtc	cgg	att	caa	gtg	caa	672	
Asp	Val	Tyr	Ala	Val	Ile	Tyr	Leu	Tyr	Val	Val	Arg	Ile	Gln	Val	Gln		
	210					215					220						
ttg	ctg	gcc	agg	cgg	gtg	gag	aag	ctg	ggc	acg	gat	gat	agt	ggc	cag	720	

Leu Leu Ala Arg Arg Val Glu Lys Leu Gly Thr Asp Asp Ser Gly Gln	
225	230 235 240
gtg gag atc tat ccc gat gag cgg cgg cag gag gag cat tgc gcg gaa	768
Val Glu Ile Tyr Pro Asp Glu Arg Arg Gln Glu Glu His Cys Ala Glu	
245	250 255
ctg cag cgc tgc att gta gat cac cag acg atg ctg cag ctg ctc gac	816
Leu Gln Arg Cys Ile Val Asp His Gln Thr Met Leu Gln Leu Leu Asp	
260	265 270
tgc att agt ccc gtc atc tcg cgt acc ata ttc gtt cag ttc ctg atc	864
Cys Ile Ser Pro Val Ile Ser Arg Thr Ile Phe Val Gln Phe Leu Ile	
275	280 285
acc gcc gcc atc atg ggc acc acc atg atc aac att ttc att ttc gcc	912
Thr Ala Ala Ile Met Gly Thr Thr Met Ile Asn Ile Phe Ile Phe Ala	
290	295 300
aat acg aac acg aag atc gca tcg atc att tac ctg ctg gcg gtg acc	960
Asn Thr Asn Thr Lys Ile Ala Ser Ile Ile Tyr Leu Leu Ala Val Thr	
305	310 315 320
ctg cag acg gct cca tgt tgc tat cag gcc acc tcg ctg atg ttg gac	1008
Leu Gln Thr Ala Pro Cys Cys Tyr Gln Ala Thr Ser Leu Met Leu Asp	
325	330 335
aac gag agg ctg gcc ctg gcc atc ttc cag tgc cag tgg ctg ggc cag	1056
Asn Glu Arg Leu Ala Leu Ala Ile Phe Gln Cys Gln Trp Leu Gly Gln	
340	345 350
agt gcc cgg ttc cgt aag atg ctg ctc tac tat ctt cat cgc gcc cag	1104
Ser Ala Arg Phe Arg Lys Met Leu Leu Tyr Tyr Leu His Arg Ala Gln	
355	360 365
cag ccc atc acg ctg acc gcc atg aag ctg ttt ccc atc aat ctg gcc	1152
Gln Pro Ile Thr Leu Thr Ala Met Lys Leu Phe Pro Ile Asn Leu Ala	
370	375 380
acg tac ttc agt ata gcc aag ttc tcg ttt tcg ctc tac acg ctc atc	1200
Thr Tyr Phe Ser Ile Ala Lys Phe Ser Phe Ser Leu Tyr Thr Leu Ile	
385	390 395 400
aag ggg atg aat ctc ggc gag cga ttc aac agg aca aat	1239
Lys Gly Met Asn Leu Gly Glu Arg Phe Asn Arg Thr Asn	
405	410

Leu Leu Ala Arg Arg Val Glu Lys Leu Gly Thr Asp Asp Ser Gly Gln
 225 230 235 240

Val Glu Ile Tyr Pro Asp Glu Arg Arg Gln Glu Glu His Cys Ala Glu
 245 250 255

Leu Gln Arg Cys Ile Val Asp His Gln Thr Met Leu Gln Leu Leu Asp
 260 265 270

Cys Ile Ser Pro Val Ile Ser Arg Thr Ile Phe Val Gln Phe Leu Ile
 275 280 285

Thr Ala Ala Ile Met Gly Thr Thr Met Ile Asn Ile Phe Ile Phe Ala
 290 295 300

Asn Thr Asn Thr Lys Ile Ala Ser Ile Ile Tyr Leu Leu Ala Val Thr
 305 310 315 320

Leu Gln Thr Ala Pro Cys Cys Tyr Gln Ala Thr Ser Leu Met Leu Asp
 325 330 335

Asn Glu Arg Leu Ala Leu Ala Ile Phe Gln Cys Gln Trp Leu Gly Gln
 340 345 350

Ser Ala Arg Phe Arg Lys Met Leu Leu Tyr Tyr Leu His Arg Ala Gln
 355 360 365

Gln Pro Ile Thr Leu Thr Ala Met Lys Leu Phe Pro Ile Asn Leu Ala
 370 375 380

Thr Tyr Phe Ser Ile Ala Lys Phe Ser Phe Ser Leu Tyr Thr Leu Ile
 385 390 395 400

Lys Gly Met Asn Leu Gly Glu Arg Phe Asn Arg Thr Asn
 405 410

<210> 73
 <211> 1089
 <212> DNA
 <213> Drosophila melanogaster

<220>
 <221> CDS
 <222> (1)..(1089)
 <223> DORLU 7.1

Introduction

147

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 Ala Val Asn Trp Tyr Leu Met Leu His Leu Ser Leu Cys Leu Arg Met
 195 200 205

ttg ggc cag cga ttg agt aag ctt cag cat gat gac aag gat ctg agg 672
 Leu Gly Gln Arg Leu Ser Lys Leu Gln His Asp Asp Lys Asp Leu Arg
 210 215 220

gag aag ttc ctg gaa ctg atc cat ctg cac cag cga ctc aag caa cag 720
 Glu Lys Phe Leu Glu Leu Ile His Leu His Gln Arg Leu Lys Gln Gln
 225 230 235 240

gcc ttg agc att gaa atc ttt att tcg aag agc acg ttc acc caa att 768
 Ala Leu Ser Ile Glu Ile Phe Ile Ser Lys Ser Thr Phe Thr Gln Ile
 245 250 255

ctg gtc agt tcc ctt atc att tgc ttc acc att tac agc atg cag atg 816
 Leu Val Ser Ser Leu Ile Ile Cys Phe Thr Ile Tyr Ser Met Gln Met
 260 265 270

tac cta gtg gcc atg atc atg cag gtc atg ctg ccc acc ata tat ggt 864
 Tyr Leu Val Ala Met Ile Met Gln Val Met Leu Pro Thr Ile Tyr Gly
 275 280 285

aac gcc gtc atc gat tct gca aat atg ttg acc gat tcc atg tac aat 912
 Asn Ala Val Ile Asp Ser Ala Asn Met Leu Thr Asp Ser Met Tyr Asn
 290 295 300

tcg gat tgg ccg gat atg aat tgc cga atg cgt cgc cta gtt tta atg 960
 Ser Asp Trp Pro Asp Met Asn Cys Arg Met Arg Arg Leu Val Leu Met
 305 310 315 320

ttt atg gtg tac tta aat cga ccg gtg acc tta aaa gcc ggt ggc ttt 1008
 Phe Met Val Tyr Leu Asn Arg Pro Val Thr Leu Lys Ala Gly Gly Phe
 325 330 335

ttt cat att ggt tta cct ctg ttt acc aag acc atg aat caa gca tac 1056
 Phe His Ile Gly Leu Pro Leu Phe Thr Lys Thr Met Asn Gln Ala Tyr
 340 345 350

agt ttg ctg gcc ttg ctg ctc aac atg aac caa 1089
 Ser Leu Leu Ala Leu Leu Leu Asn Met Asn Gln
 355 360

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<211> 363

<212> PRT

<213> Drosophila melanogaster

<400> 74

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Lys Trp Trp Arg Leu Trp Pro Arg Lys Glu Ser Val Ser Thr Pro Asp
20 25 30

Trp Thr Asn Trp Gln Ala Tyr Ala Leu His Val Pro Phe Thr Phe Leu
35 40 45

Phe Val Leu Leu Leu Trp Leu Glu Ala Ile Lys Ser Arg Asp Ile Gln
50 55 60

His Thr Ala Asp Val Leu Leu Ile Cys Leu Thr Thr Thr Ala Leu Gly
65 70 75 80

Gly Lys Val Ile Asn Ile Trp Lys Tyr Ala His Val Ala Gln Gly Ile
85 90 95

Leu Ser Glu Trp Ser Thr Trp Asp Leu Phe Glu Leu Arg Ser Lys Gln
100 105 110

Glu Val Asp Met Trp Arg Phe Glu His Arg Arg Phe Asn Arg Val Phe
115 120 125

Met Phe Tyr Cys Leu Cys Ser Ala Gly Val Ile Pro Phe Ile Val Ile
130 135 140

Gln Pro Leu Phe Asp Ile Pro Asn Arg Leu Pro Phe Trp Met Trp Thr
145 150 155 160

Pro Phe Asp Trp Gln Gln Pro Val Leu Leu Trp Tyr Ala Phe Ile Tyr
165 170 175

Gln Ala Thr Thr Ile Pro Ile Ala Cys Ala Cys Asn Val Thr Met Asp
180 185 190

Ala Val Asn Trp Tyr Leu Met Leu His Leu Ser Leu Cys Leu Arg Met
195 200 205

Leu Gly Gln Arg Leu Ser Lys Leu Gln His Asp Asp Lys Asp Leu Arg
210 215 220

Glu Lys Phe Leu Glu Leu Ile His Leu His Gln Arg Leu Lys Gln Gln
225 230 235 240

Ala Leu Ser Ile Glu Ile Phe Ile Ser Lys Ser Thr Phe Thr Gln Ile
 245 250 255

Leu Val Ser Ser Leu Ile Ile Cys Phe Thr Ile Tyr Ser Met Gln Met
 260 265 270

Tyr Leu Val Ala Met Ile Met Gln Val Met Leu Pro Thr Ile Tyr Gly
 275 280 285

Asn Ala Val Ile Asp Ser Ala Asn Met Leu Thr Asp Ser Met Tyr Asn
 290 295 300

Ser Asp Trp Pro Asp Met Asn Cys Arg Met Arg Arg Leu Val Leu Met
 305 310 315 320

Phe Met Val Tyr Leu Asn Arg Pro Val Thr Leu Lys Ala Gly Gly Phe
 325 330 335

Phe His Ile Gly Leu Pro Leu Phe Thr Lys Thr Met Asn Gln Ala Tyr
 340 345 350

Ser Leu Leu Ala Leu Leu Leu Asn Met Asn Gln
 355 360

<210> 75
 <211> 1176
 <212> DNA
 <213> Drosophila melanogaster

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 <222> (1)..(1176)
 <223> DORLU 9.1

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 atg agc gac aag gtg aag gga aaa aag cag gag gaa aag gat caa tcc 48
 Met Ser Asp Lys Val Lys Gly Lys Lys Gln Glu Glu Lys Asp Gln Ser
 1 5 10 15

ttg cgg gtg caa att ctc gtt tat cgc tgc atg ggc atc gat ttg tgg 96
 Leu Arg Val Gln Ile Leu Val Tyr Arg Cys Met Gly Ile Asp Leu Trp
 20 25 30

agc ccc acg atg gcg aat gac cgc ccg tgg ctg acc ttt gtc aca atg 144
 Ser Pro Thr Met Ala Asn Asp Arg Pro Trp Leu Thr Phe Val Thr Met

35

40

45

gga cca ctt ttc ctg ttt atg gtg ccc atg ttc ctg gcc gcc cac gag 192
 Gly Pro Leu Phe Leu Phe Met Val Pro Met Phe Leu Ala Ala His Glu
 50 55 60

tac atc acc cag gtg agc ctg ctc tcc gac acc ctg ggc tcc acc ttc 240
 Tyr Ile Thr Gln Val Ser Leu Leu Ser Asp Thr Leu Gly Ser Thr Phe
 65 70 75 80

gcc agc atg ctc acc ctg gtc aaa ttc ctg ctc ttc tgc tat cat cgc 288
 Ala Ser Met Leu Thr Leu Val Lys Phe Leu Leu Phe Cys Tyr His Arg
 85 90 95

aag gag ttc gtc ggc ctg atc tac cac atc agg gcc att ctg gct aaa 336
 Lys Glu Phe Val Gly Leu Ile Tyr His Ile Arg Ala Ile Leu Ala Lys
 100 105 110

gaa atc gaa gtg tgg cct gat gcg cgg gaa atc atc gag gtg gag aac 384
 Glu Ile Glu Val Trp Pro Asp Ala Arg Glu Ile Ile Glu Val Glu Asn
 115 120 125

caa agt gac caa atg ctc agt ctt acg tac act cgc tgt ttt gga ctg 432
 Gln Ser Asp Gln Met Leu Ser Leu Thr Tyr Thr Arg Cys Phe Gly Leu
 130 135 140

gct gga atc ttt gcg gcc ctg aag ccc ttt gtg ggc atc ata ctc tcc 480
 Ala Gly Ile Phe Ala Ala Leu Lys Pro Phe Val Gly Ile Ile Leu Ser
 145 150 155 160

tcg att cgc ggc gac gag att cac ctg gag ctg ccc cac aac ggc gtt 528
 Ser Ile Arg Gly Asp Glu Ile His Leu Glu Leu Pro His Asn Gly Val
 165 170 175

tac ccg tac gat ctc cag gtg gtc atg ttt tat gtg ccc acc tat ctg 576
 Tyr Pro Tyr Asp Leu Gln Val Val Met Phe Tyr Val Pro Thr Tyr Leu
 180 185 190

tgg aat gtg atg gcc agc tat agt gct gta acc atg gca ctc tgc gtg 624
 Trp Asn Val Met Ala Ser Tyr Ser Ala Val Thr Met Ala Leu Cys Val
 195 200 205

gac tcg ctg ctc ttc ttt ttc acc tac aac gtg tgc gcc att ttc aag 672
 Asp Ser Leu Leu Phe Phe Phe Thr Tyr Asn Val Cys Ala Ile Phe Lys
 210 215 220

atc gcc aag cac cgg atg atc cat ctg ccg gcg gtg ggc gga aag gag 720
 Ile Ala Lys His Arg Met Ile His Leu Pro Ala Val Gly Gly Lys Glu

225	230	235	240	
gag ctg gag ggg ctc gtc cag gtg ctg ctg ctg cac cag aag ggc ctc				768
Glu Leu Glu Gly Leu Val Gln Val Leu Leu Leu His Gln Lys Gly Leu				
245		250	255	
cag atc gcc gat cac att gcg gac aag tac cgg ccg ctg atc ttt ttg				816
Gln Ile Ala Asp His Ile Ala Asp Lys Tyr Arg Pro Leu Ile Phe Leu				
260		265	270	
cag ttc ttt ctg tcc gcc ttg cag atc tgc ttc att gga ttc cag gtg				864
Gln Phe Phe Leu Ser Ala Leu Gln Ile Cys Phe Ile Gly Phe Gln Val				
275		280	285	
gct gat ctg ttt ccc aat ccg cag agt ctc tac ttt atc gcc ttt gtg				912
Ala Asp Leu Phe Pro Asn Pro Gln Ser Leu Tyr Phe Ile Ala Phe Val				
290		295	300	
ggc tcg ctg ctc atc gca ctg ttc atc tac tcg aag tgc ggc gaa aat				960
Gly Ser Leu Leu Ile Ala Leu Phe Ile Tyr Ser Lys Cys Gly Glu Asn				
305		310	315	320
atc aag agt gcc agc ctg gat ttc gga aac ggg ctg tac gag acc aac				1008
Ile Lys Ser Ala Ser Leu Asp Phe Gly Asn Gly Leu Tyr Glu Thr Asn				
325		330	335	
tgg acc gac ttc tcg cca ccc act aaa aga gcc ctc ctc att gcc gcc				1056
Trp Thr Asp Phe Ser Pro Pro Thr Lys Arg Ala Leu Leu Ile Ala Ala				
340		345	350	
atg cgc gcc cag cga cct tgc cag atg aag ggc tac ttt ttc gag gcc				1104
Met Arg Ala Gln Arg Pro Cys Gln Met Lys Gly Tyr Phe Phe Glu Ala				
355		360	365	
agc atg gcc acc ttc tcg acg att gtt cgc tct gcc gtg tcg tac atc				1152
Ser Met Ala Thr Phe Ser Thr Ile Val Arg Ser Ala Val Ser Tyr Ile				
370		375	380	
atg atg ttg cgc tcc ttt aat gcc				1176
Met Met Leu Arg Ser Phe Asn Ala				
385		390		

<210> 76

<211> 392

<212> PRT

<213> Drosophila melanogaster

<400> 76

Met Ser Asp Lys Val Lys Gly Lys Lys Gln Glu Glu Lys Asp Gln Ser
1 5 10 15

Leu Arg Val Gln Ile Leu Val Tyr Arg Cys Met Gly Ile Asp Leu Trp
20 25 30

Ser Pro Thr Met Ala Asn Asp Arg Pro Trp Leu Thr Phe Val Thr Met
35 40 45

Gly Pro Leu Phe Leu Phe Met Val Pro Met Phe Leu Ala Ala His Glu
50 55 60

Tyr Ile Thr Gln Val Ser Leu Leu Ser Asp Thr Leu Gly Ser Thr Phe
65 70 75 80

Ala Ser Met Leu Thr Leu Val Lys Phe Leu Leu Phe Cys Tyr His Arg
85 90 95

Lys Glu Phe Val Gly Leu Ile Tyr His Ile Arg Ala Ile Leu Ala Lys
100 105 110

Glu Ile Glu Val Trp Pro Asp Ala Arg Glu Ile Ile Glu Val Glu Asn
115 120 125

Gln Ser Asp Gln Met Leu Ser Leu Thr Tyr Thr Arg Cys Phe Gly Leu
130 135 140

Ala Gly Ile Phe Ala Ala Leu Lys Pro Phe Val Gly Ile Ile Leu Ser
145 150 155 160

Ser Ile Arg Gly Asp Glu Ile His Leu Glu Leu Pro His Asn Gly Val
165 170 175

Tyr Pro Tyr Asp Leu Gln Val Val Met Phe Tyr Val Pro Thr Tyr Leu
180 185 190

Trp Asn Val Met Ala Ser Tyr Ser Ala Val Thr Met Ala Leu Cys Val
195 200 205

Asp Ser Leu Leu Phe Phe Phe Thr Tyr Asn Val Cys Ala Ile Phe Lys
210 215 220

Ile Ala Lys His Arg Met Ile His Leu Pro Ala Val Gly Gly Lys Glu
225 230 235 240

Glu Leu Glu Gly Leu Val Gln Val Leu Leu Leu His Gln Lys Gly Leu
245 250 255

Gln Ile Ala Asp His Ile Ala Asp Lys Tyr Arg Pro Leu Ile Phe Leu
 260 265 270

Gln Phe Phe Leu Ser Ala Leu Gln Ile Cys Phe Ile Gly Phe Gln Val
 275 280 285

Ala Asp Leu Phe Pro Asn Pro Gln Ser Leu Tyr Phe Ile Ala Phe Val
 290 295 300

Gly Ser Leu Leu Ile Ala Leu Phe Ile Tyr Ser Lys Cys Gly Glu Asn
 305 310 315 320

Ile Lys Ser Ala Ser Leu Asp Phe Gly Asn Gly Leu Tyr Glu Thr Asn
 325 330 335

Trp Thr Asp Phe Ser Pro Pro Thr Lys Arg Ala Leu Leu Ile Ala Ala
 340 345 350

Met Arg Ala Gln Arg Pro Cys Gln Met Lys Gly Tyr Phe Phe Glu Ala
 355 360 365

Ser Met Ala Thr Phe Ser Thr Ile Val Arg Ser Ala Val Ser Tyr Ile
 370 375 380

Met Met Leu Arg Ser Phe Asn Ala
 385 390

<210> 77

<211> 1221

<212> DNA

<213> Drosophila melanogaster

<220>

<221> CDS

<222> (1)..(1221)

<223> DORLU 12.1

<400> 77

atg gat aac gtc gcg gaa atg cct gaa gaa aag tat gtc gaa gtc gat 48
 Met Asp Asn Val Ala Glu Met Pro Glu Glu Lys Tyr Val Glu Val Asp
 1 5 10 15

gat ttt ttg agg cta gct gtg aaa ttc tac aat act ttg ggc att gat 96
 Asp Phe Leu Arg Leu Ala Val Lys Phe Tyr Asn Thr Leu Gly Ile Asp
 20 25 30

ccc tat gaa act gga cga aaa cga act att tgg ttt caa ata tat ttc	144
Pro Tyr Glu Thr Gly Arg Lys Arg Thr Ile Trp Phe Gln Ile Tyr Phe	
35 40 45	
gca ttg aat atg ttt aat atg gtg ttt agt ttt tat gcc gag gta gcg	192
Ala Leu Asn Met Phe Asn Met Val Phe Ser Phe Tyr Ala Glu Val Ala	
50 55 60	
act ctg gtg gac agg tta cgc gat aat gaa aat ttt ctc gag agc tgc	240
Thr Leu Val Asp Arg Leu Arg Asp Asn Glu Asn Phe Leu Glu Ser Cys	
65 70 75 80	
atc tta ctg agc tac gtg tcc ttt gtg gtc atg ggc ctc tcc aag ata	288
Ile Leu Leu Ser Tyr Val Ser Phe Val Val Met Gly Leu Ser Lys Ile	
85 90 95	
ggt gct gta atg aaa aaa aag cca aaa atg aca gct ttg gtc agg caa	336
Gly Ala Val Met Lys Lys Lys Pro Lys Met Thr Ala Leu Val Arg Gln	
100 105 110	
ttg gag acc tgc ttt ccg tcg cca agt gca aag gtt caa gag gaa tat	384
Leu Glu Thr Cys Phe Pro Ser Pro Ser Ala Lys Val Gln Glu Glu Tyr	
115 120 125	
gct gtg aag tcc tgg ctg aaa cgc tgc cat ata tac aca aag gga ttt	432
Ala Val Lys Ser Trp Leu Lys Arg Cys His Ile Tyr Thr Lys Gly Phe	
130 135 140	
ggt ggt ctc ttc atg atc atg tat ttc gct cac gct ctg att ccc tta	480
Gly Gly Leu Phe Met Ile Met Tyr Phe Ala His Ala Leu Ile Pro Leu	
145 150 155 160	
ttc ata tac ttc att caa aga gtg ctg ctc cac tat ccg gat gcc aag	528
Phe Ile Tyr Phe Ile Gln Arg Val Leu Leu His Tyr Pro Asp Ala Lys	
165 170 175	
cag att atg ccg ttt tac caa ctc gaa cct tgg gaa ttt cgc gac tcc	576
Gln Ile Met Pro Phe Tyr Gln Leu Glu Pro Trp Glu Phe Arg Asp Ser	
180 185 190	
tgg ttg ttt tat cca agc tat ttt cac cag tcg tcg gcc gga tat acg	624
Trp Leu Phe Tyr Pro Ser Tyr Phe His Gln Ser Ser Ala Gly Tyr Thr	
195 200 205	
gct aca tgt gga tcc att gcc ggt gac cta atg atc ttc gct gtg gtc	672
Ala Thr Cys Gly Ser Ile Ala Gly Asp Leu Met Ile Phe Ala Val Val	
210 215 220	

<210> 78
 <211> 407
 <212> PRT
 <213> Drosophila melanogaster

<400> 78

Met Asp Asn Val Ala Glu Met Pro Glu Glu Lys Tyr Val Glu Val Asp
 1 5 10 15

Asp Phe Leu Arg Leu Ala Val Lys Phe Tyr Asn Thr Leu Gly Ile Asp
 20 25 30

Pro Tyr Glu Thr Gly Arg Lys Arg Thr Ile Trp Phe Gln Ile Tyr Phe
 35 40 45

Ala Leu Asn Met Phe Asn Met Val Phe Ser Phe Tyr Ala Glu Val Ala
 50 55 60

Thr Leu Val Asp Arg Leu Arg Asp Asn Glu Asn Phe Leu Glu Ser Cys
 65 70 75 80

Ile Leu Leu Ser Tyr Val Ser Phe Val Val Met Gly Leu Ser Lys Ile
 85 90 95

Gly Ala Val Met Lys Lys Lys Pro Lys Met Thr Ala Leu Val Arg Gln
 100 105 110

Leu Glu Thr Cys Phe Pro Ser Pro Ser Ala Lys Val Gln Glu Glu Tyr
 115 120 125

Ala Val Lys Ser Trp Leu Lys Arg Cys His Ile Tyr Thr Lys Gly Phe
 130 135 140

Gly Gly Leu Phe Met Ile Met Tyr Phe Ala His Ala Leu Ile Pro Leu
 145 150 155 160

Phe Ile Tyr Phe Ile Gln Arg Val Leu Leu His Tyr Pro Asp Ala Lys
 165 170 175

Gln Ile Met Pro Phe Tyr Gln Leu Glu Pro Trp Glu Phe Arg Asp Ser
 180 185 190

Trp Leu Phe Tyr Pro Ser Tyr Phe His Gln Ser Ser Ala Gly Tyr Thr
 195 200 205

Ala Thr Cys Gly Ser Ile Ala Gly Asp Leu Met Ile Phe Ala Val Val

210 215 220
 Leu Gln Val Ile Met His Tyr Glu Arg Leu Ala Lys Val Leu Arg Glu
 225 230 235 240
 Phe Lys Ile Gln Ala His Asn Ala Pro Asn Gly Ala Lys Glu Asp Ile
 245 250 255
 Arg Lys Leu Gln Ser Leu Val Ala Asn His Ile Asp Ile Leu Arg Leu
 260 265 270
 Thr Asp Leu Met Asn Glu Val Phe Gly Ile Pro Leu Leu Leu Asn Phe
 275 280 285
 Ile Ala Ser Ala Leu Leu Val Cys Leu Val Gly Val Gln Leu Thr Ile
 290 295 300
 Ala Leu Ser Pro Glu Tyr Phe Cys Lys Gln Met Leu Phe Leu Ile Ser
 305 310 315 320
 Val Leu Leu Glu Val Tyr Leu Leu Cys Ser Phe Ser Gln Arg Leu Ile
 325 330 335
 Asp Ala Ser Glu Asn Val Gly His Ala Ala Tyr Asp Met Asp Trp Leu
 340 345 350
 Gly Ser Asp Lys Arg Phe Lys Lys Ile Leu Ile Phe Ile Ser Met Arg
 355 360 365
 Ser Gln Lys Pro Val Cys Leu Lys Ala Thr Val Val Leu Asp Leu Ser
 370 375 380
 Met Pro Thr Met Ser Ile Phe Leu Gly Met Ser Tyr Lys Phe Phe Cys
 385 390 395 400
 Ala Val Arg Thr Met Tyr Gln
 405

<210> 79
 <211> 1212
 <212> DNA
 <213> Drosophila melanogaster

<220>
 <221> CDS
 <222> (1)..(1212)

<223> DORLU 13.1

<400> 79

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Met Glu Thr Ala Lys Asp Asn Thr Ala Arg Thr Phe Met Glu Leu Met	
1 5 10 15	
cga gtg cca gta cag ttt tac aga acg att gga gag gat atc tac gcc	96
Arg Val Pro Val Gln Phe Tyr Arg Thr Ile Gly Glu Asp Ile Tyr Ala	
20 25 30	
cat cga tcc acg aat ccc cta aaa tcg ctt ctc ttc aag atc tat cta	144
His Arg Ser Thr Asn Pro Leu Lys Ser Leu Leu Phe Lys Ile Tyr Leu	
35 40 45	
tat gcg gga ttc ata aat ttt aat ctg ttg gta atc ggt gaa ctg gtg	192
Tyr Ala Gly Phe Ile Asn Phe Asn Leu Leu Val Ile Gly Glu Leu Val	
50 55 60	
ttc ttc tac aac tca att cag gac ttt gaa acc att cga ttg gcc atc	240
Phe Phe Tyr Asn Ser Ile Gln Asp Phe Glu Thr Ile Arg Leu Ala Ile	
65 70 75 80	
gcg gtg gct cca tgt atc gga ttt tct ctg gtt gct gat ttt aaa caa	288
Ala Val Ala Pro Cys Ile Gly Phe Ser Leu Val Ala Asp Phe Lys Gln	
85 90 95	
gct gcc atg att aga ggc aag aaa aca cta att atg cta ctc gat gat	336
Ala Ala Met Ile Arg Gly Lys Lys Thr Leu Ile Met Leu Leu Asp Asp	
100 105 110	
ttg gag aac atg cat ccg aaa acc ctg gca aag caa atg gaa tac aaa	384
Leu Glu Asn Met His Pro Lys Thr Leu Ala Lys Gln Met Glu Tyr Lys	
115 120 125	
ttg ccg gac ttt gaa aag acc atg aaa cgt gtg atc aat ata ttc acc	432
Leu Pro Asp Phe Glu Lys Thr Met Lys Arg Val Ile Asn Ile Phe Thr	
130 135 140	
ttt ctc tgc ttg gcc tat acg act acg ttc tcc ttt tat ccg gcc atc	480
Phe Leu Cys Leu Ala Tyr Thr Thr Thr Phe Ser Phe Tyr Pro Ala Ile	
145 150 155 160	
aag gca tcc gtg aaa ttt aat ttc ttg ggc tac gac acc ttt gat cga	528
Lys Ala Ser Val Lys Phe Asn Phe Leu Gly Tyr Asp Thr Phe Asp Arg	
165 170 175	
aat ttt ggt ttc ctc atc tgg ttt ccc ttc gat gca aca agg aat aat	576

Asn Phe Gly Phe Leu Ile Trp Phe Pro Phe Asp Ala Thr Arg Asn Asn	
180 185 190	
ttg ata tac tgg atc atg tac tgg gac ata gcc cat ggg gcc tat cta	624
Leu Ile Tyr Trp Ile Met Tyr Trp Asp Ile Ala His Gly Ala Tyr Leu	
195 200 205	
gcg ggt att gct ttt ctc tgc gcc gat ctt ttg ctc gtc gta gtc att	672
Ala Gly Ile Ala Phe Leu Cys Ala Asp Leu Leu Leu Val Val Val Ile	
210 215 220	
acc cag att tgt atg cac ttt aac tat ata tct atg cga tta gag gat	720
Thr Gln Ile Cys Met His Phe Asn Tyr Ile Ser Met Arg Leu Glu Asp	
225 230 235 240	
cat cca tgt aat tcg aat gag gac aaa gag aat ata gag ttt ctt att	768
His Pro Cys Asn Ser Asn Glu Asp Lys Glu Asn Ile Glu Phe Leu Ile	
245 250 255	
ggc att atc aga tac cat gac aag tgc ctt aaa cta tgc gaa cat gtc	816
Gly Ile Ile Arg Tyr His Asp Lys Cys Leu Lys Leu Cys Glu His Val	
260 265 270	
aac gat ctg tat agt ttc tct ttg ctg ctt aat ttc ctt atg gca tcc	864
Asn Asp Leu Tyr Ser Phe Ser Leu Leu Leu Asn Phe Leu Met Ala Ser	
275 280 285	
atg cag att tgt ttc ata gcc ttt cag gtc acc gaa tca aca gtg gaa	912
Met Gln Ile Cys Phe Ile Ala Phe Gln Val Thr Glu Ser Thr Val Glu	
290 295 300	
gtg att att att tac tgc att ttt ttg atg acc tcg atg gtt cag gta	960
Val Ile Ile Ile Tyr Cys Ile Phe Leu Met Thr Ser Met Val Gln Val	
305 310 315 320	
ttt atg gtg tgc tac tat ggg gat act tta att gcc gcg agc ttg aaa	1008
Phe Met Val Cys Tyr Tyr Gly Asp Thr Leu Ile Ala Ala Ser Leu Lys	
325 330 335	
gtg ggc gat gcc gct tac aac caa aag tgg ttt cag tgc agc aaa tcc	1056
Val Gly Asp Ala Ala Tyr Asn Gln Lys Trp Phe Gln Cys Ser Lys Ser	
340 345 350	
tat tgc acc atg ttg aag ttg cta atc atg agg agt cag aaa cca gct	1104
Tyr Cys Thr Met Leu Lys Leu Leu Ile Met Arg Ser Gln Lys Pro Ala	
355 360 365	
tca ata aga ccg ccg act ttt ccc ccc ata tcc ttg gtt acc tat atg	1152

Asn	Phe	Gly	Phe	Leu	Ile	Trp	Phe	Pro	Phe	Asp	Ala	Thr	Arg	Asn	Asn
			180					185					190		
Leu	Ile	Tyr	Trp	Ile	Met	Tyr	Trp	Asp	Ile	Ala	His	Gly	Ala	Tyr	Leu
		195					200					205			
Ala	Gly	Ile	Ala	Phe	Leu	Cys	Ala	Asp	Leu	Leu	Leu	Val	Val	Val	Ile
	210					215					220				
Thr	Gln	Ile	Cys	Met	His	Phe	Asn	Tyr	Ile	Ser	Met	Arg	Leu	Glu	Asp
225					230					235					240
His	Pro	Cys	Asn	Ser	Asn	Glu	Asp	Lys	Glu	Asn	Ile	Glu	Phe	Leu	Ile
			245						250					255	
Gly	Ile	Ile	Arg	Tyr	His	Asp	Lys	Cys	Leu	Lys	Leu	Cys	Glu	His	Val
			260					265					270		
Asn	Asp	Leu	Tyr	Ser	Phe	Ser	Leu	Leu	Leu	Asn	Phe	Leu	Met	Ala	Ser
		275					280					285			
Met	Gln	Ile	Cys	Phe	Ile	Ala	Phe	Gln	Val	Thr	Glu	Ser	Thr	Val	Glu
	290					295					300				
Val	Ile	Ile	Ile	Tyr	Cys	Ile	Phe	Leu	Met	Thr	Ser	Met	Val	Gln	Val
305					310					315					320
Phe	Met	Val	Cys	Tyr	Tyr	Gly	Asp	Thr	Leu	Ile	Ala	Ala	Ser	Leu	Lys
			325						330					335	
Val	Gly	Asp	Ala	Ala	Tyr	Asn	Gln	Lys	Trp	Phe	Gln	Cys	Ser	Lys	Ser
			340					345					350		
Tyr	Cys	Thr	Met	Leu	Lys	Leu	Leu	Ile	Met	Arg	Ser	Gln	Lys	Pro	Ala
		355					360					365			
Ser	Ile	Arg	Pro	Pro	Thr	Phe	Pro	Pro	Ile	Ser	Leu	Val	Thr	Tyr	Met
	370					375					380				
Lys	Val	Ile	Ser	Met	Ser	Tyr	Gln	Phe	Phe	Ala	Leu	Leu	Arg	Thr	Thr
385					390					395					400
Tyr	Ser	Asn	Asn												

<210> 81
 <211> 1179
 <212> DNA
 <213> Drosophila melanogaster

<220>
 <221> CDS
 <222> (1)..(1179)
 <223> DORLU 14.1

<400> 81
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 Met Glu Pro Val Gln Tyr Ser Tyr Glu Asp Phe Ala Arg Leu Pro Thr
 1 5 10 15
 acg gtg ttc tgg atc atg ggc tac gac atg ctg ggc gtt ccg aag acc 96
 Thr Val Phe Trp Ile Met Gly Tyr Asp Met Leu Gly Val Pro Lys Thr
 20 25 30
 cgc tct cgc agg ata cta tac tgg ata tat cgt ttc ctc tgt ctc gcc 144
 Arg Ser Arg Arg Ile Leu Tyr Trp Ile Tyr Arg Phe Leu Cys Leu Ala
 35 40 45
 agc cat ggg gtc tgt gta gga gtc atg gta ttt cgt atg gtg gag gca 192
 Ser His Gly Val Cys Val Gly Val Met Val Phe Arg Met Val Glu Ala
 50 55 60
 aag acc att gac aat gtt tcg ctg atc atg cgg tat gcc act ctg gtc 240
 Lys Thr Ile Asp Asn Val Ser Leu Ile Met Arg Tyr Ala Thr Leu Val
 65 70 75 80
 acc tat atc atc aac tcg gat acg aaa ttc gca act gtc tta caa agg 288
 Thr Tyr Ile Ile Asn Ser Asp Thr Lys Phe Ala Thr Val Leu Gln Arg
 85 90 95
 agt gca att caa agt cta aac tca aaa ctg gcc gaa cta tat ccg aag 336
 Ser Ala Ile Gln Ser Leu Asn Ser Lys Leu Ala Glu Leu Tyr Pro Lys
 100 105 110
 acc acg ctg gac agg atc tat cac cgg gtg aat gat cac tat tgg acc 384
 Thr Thr Leu Asp Arg Ile Tyr His Arg Val Asn Asp His Tyr Trp Thr
 115 120 125
 aag tca ttt gta tat ttg gtt att atc tac att ggt tcg tcg att atg 432
 Lys Ser Phe Val Tyr Leu Val Ile Ile Tyr Ile Gly Ser Ser Ile Met
 130 135 140

gtt	gtt	att	gga	ccg	att	att	acg	tcg	att	ata	gct	tac	ttc	acg	cac	480
Val	Val	Ile	Gly	Pro	Ile	Ile	Thr	Ser	Ile	Ile	Ala	Tyr	Phe	Thr	His	
145					150					155					160	
aac	gtt	ttc	acc	tac	atg	cac	tgc	tat	ccg	tac	ttt	ttg	tat	gat	cct	528
Asn	Val	Phe	Thr	Tyr	Met	His	Cys	Tyr	Pro	Tyr	Phe	Leu	Tyr	Asp	Pro	
				165					170					175		
gag	aag	gat	ccg	gtt	tgg	atc	tac	atc	agc	atc	tat	gct	ctg	gaa	tgg	576
Glu	Lys	Asp	Pro	Val	Trp	Ile	Tyr	Ile	Ser	Ile	Tyr	Ala	Leu	Glu	Trp	
			180					185					190			
ttg	cac	agc	aca	cag	atg	gtc	att	tcg	aac	att	ggc	gcg	gat	atc	tgg	624
Leu	His	Ser	Thr	Gln	Met	Val	Ile	Ser	Asn	Ile	Gly	Ala	Asp	Ile	Trp	
		195					200					205				
ctg	ctg	tac	ttt	cag	gtg	cag	ata	aat	ctc	cac	ttc	agg	ggc	att	ata	672
Leu	Leu	Tyr	Phe	Gln	Val	Gln	Ile	Asn	Leu	His	Phe	Arg	Gly	Ile	Ile	
	210					215					220					
cga	tca	ctg	gcg	gat	cac	aag	ccc	agt	gtg	aag	cac	gac	cag	gag	gac	720
Arg	Ser	Leu	Ala	Asp	His	Lys	Pro	Ser	Val	Lys	His	Asp	Gln	Glu	Asp	
225					230					235					240	
agg	aaa	ttc	att	gcg	aaa	att	gtc	gac	aag	cag	gtg	cac	ctg	gtc	agt	768
Arg	Lys	Phe	Ile	Ala	Lys	Ile	Val	Asp	Lys	Gln	Val	His	Leu	Val	Ser	
				245					250					255		
ttg	caa	aac	gat	ctg	aat	ggt	atc	ttt	gga	aaa	tcg	ctg	ctt	cta	agc	816
Leu	Gln	Asn	Asp	Leu	Asn	Gly	Ile	Phe	Gly	Lys	Ser	Leu	Leu	Leu	Ser	
			260					265					270			
ctg	ctg	acc	acc	gca	gcg	gtt	atc	tgc	acg	gtg	gcg	gtg	tac	act	ctg	864
Leu	Leu	Thr	Thr	Ala	Ala	Val	Ile	Cys	Thr	Val	Ala	Val	Tyr	Thr	Leu	
		275					280					285				
att	cag	ggt	ccc	acc	ttg	gag	ggc	ttc	acc	tat	gtg	atc	ttc	atc	ggg	912
Ile	Gln	Gly	Pro	Thr	Leu	Glu	Gly	Phe	Thr	Tyr	Val	Ile	Phe	Ile	Gly	
	290					295					300					
act	tct	gtg	atg	cag	gtc	tac	ctg	gtg	tgc	tat	tac	ggt	cag	caa	gtt	960
Thr	Ser	Val	Met	Gln	Val	Tyr	Leu	Val	Cys	Tyr	Tyr	Gly	Gln	Gln	Val	
305					310					315					320	
ctc	gac	ttg	gtg	gag	cgc	gag	gtg	gcc	cac	gcc	gtg	tac	aat	cat	gat	1008
Leu	Asp	Leu	Val	Glu	Arg	Glu	Val	Ala	His	Ala	Val	Tyr	Asn	His	Asp	
				325				330						335		

ttt cac gat gct tct ata gcg tac aag agg tac ctg ctc ata atc att 1056
Phe His Asp Ala Ser Ile Ala Tyr Lys Arg Tyr Leu Leu Ile Ile Ile
340 345 350

atc agg gcg cag cag ccc gtg gaa ctt aat gcc atg ggc tac ctg tcc 1104
Ile Arg Ala Gln Gln Pro Val Glu Leu Asn Ala Met Gly Tyr Leu Ser
355 360 365

att tcg ctg gac acc ttt aaa cag ctg atg agc gtc tcc tac cgg gtt 1152
Ile Ser Leu Asp Thr Phe Lys Gln Leu Met Ser Val Ser Tyr Arg Val
370 375 380

ata acc atg ctc atg cag atg att cag 1179
Ile Thr Met Leu Met Gln Met Ile Gln
385 390

<210> 82

<211> 393

<212> PRT

<213> Drosophila melanogaster

<400> 82

Met Glu Pro Val Gln Tyr Ser Tyr Glu Asp Phe Ala Arg Leu Pro Thr
1 5 10 15

Thr Val Phe Trp Ile Met Gly Tyr Asp Met Leu Gly Val Pro Lys Thr
20 25 30

Arg Ser Arg Arg Ile Leu Tyr Trp Ile Tyr Arg Phe Leu Cys Leu Ala
35 40 45

Ser His Gly Val Cys Val Gly Val Met Val Phe Arg Met Val Glu Ala
50 55 60

Lys Thr Ile Asp Asn Val Ser Leu Ile Met Arg Tyr Ala Thr Leu Val
65 70 75 80

Thr Tyr Ile Ile Asn Ser Asp Thr Lys Phe Ala Thr Val Leu Gln Arg
85 90 95

Ser Ala Ile Gln Ser Leu Asn Ser Lys Leu Ala Glu Leu Tyr Pro Lys
100 105 110

Thr Thr Leu Asp Arg Ile Tyr His Arg Val Asn Asp His Tyr Trp Thr
115 120 125

Lys Ser Phe Val Tyr Leu Val Ile Ile Tyr Ile Gly Ser Ser Ile Met

130	135	140																	
Val Val Ile Gly Pro Ile Ile Thr Ser Ile Ile Ala Tyr Phe Thr His																			
145	150	155																	160
Asn Val Phe Thr Tyr Met His Cys Tyr Pro Tyr Phe Leu Tyr Asp Pro																			
	165							170											175
Glu Lys Asp Pro Val Trp Ile Tyr Ile Ser Ile Tyr Ala Leu Glu Trp																			
	180						185												190
Leu His Ser Thr Gln Met Val Ile Ser Asn Ile Gly Ala Asp Ile Trp																			
	195						200						205						
Leu Leu Tyr Phe Gln Val Gln Ile Asn Leu His Phe Arg Gly Ile Ile																			
	210					215						220							
Arg Ser Leu Ala Asp His Lys Pro Ser Val Lys His Asp Gln Glu Asp																			
225					230					235									240
Arg Lys Phe Ile Ala Lys Ile Val Asp Lys Gln Val His Leu Val Ser																			
				245					250										255
Leu Gln Asn Asp Leu Asn Gly Ile Phe Gly Lys Ser Leu Leu Leu Ser																			
				260				265											270
Leu Leu Thr Thr Ala Ala Val Ile Cys Thr Val Ala Val Tyr Thr Leu																			
				275				280											285
Ile Gln Gly Pro Thr Leu Glu Gly Phe Thr Tyr Val Ile Phe Ile Gly																			
				290				295					300						
Thr Ser Val Met Gln Val Tyr Leu Val Cys Tyr Tyr Gly Gln Gln Val																			
305					310					315									320
Leu Asp Leu Val Glu Arg Glu Val Ala His Ala Val Tyr Asn His Asp																			
				325				330											335
Phe His Asp Ala Ser Ile Ala Tyr Lys Arg Tyr Leu Leu Ile Ile Ile																			
				340				345											350
Ile Arg Ala Gln Gln Pro Val Glu Leu Asn Ala Met Gly Tyr Leu Ser																			
				355				360					365						
Ile Ser Leu Asp Thr Phe Lys Gln Leu Met Ser Val Ser Tyr Arg Val																			
				370				375					380						
Ile Thr Met Leu Met Gln Met Ile Gln																			

385

390

<210> 83

<211> 1134

<212> DNA

<213> Drosophila melanogaster

<220>

<221> CDS

<222> (1)..(1134)

<223> DORLU 15.1

<400> 83

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Met Asp Ala Ser Tyr Phe Ala Val Gln Arg Arg Ala Leu Glu Ile Val	
1 5 10 15	

gga ttc gat ccc agt act ccg caa ctg agt ctg aaa cat ccc atc tgg	96
Gly Phe Asp Pro Ser Thr Pro Gln Leu Ser Leu Lys His Pro Ile Trp	
20 25 30	

gcc ggg att ctc atc ctg tcc ttg atc tct cac aac tgg ccc atg gta	144
Ala Gly Ile Leu Ile Leu Ser Leu Ile Ser His Asn Trp Pro Met Val	
35 40 45	

gtc tat gcc ctg cag gat ctc tcc gac ttg acc cgt ctg acg gac aac	192
Val Tyr Ala Leu Gln Asp Leu Ser Asp Leu Thr Arg Leu Thr Asp Asn	
50 55 60	

ttt gcg gtg ttt atg caa gga tca cag agc acc ttc aag ttc ctg gtc	240
Phe Ala Val Phe Met Gln Gly Ser Gln Ser Thr Phe Lys Phe Leu Val	
65 70 75 80	

atg atg gcg aaa cga agg cgc att gga tcg ttg att cac cgt ttg cat	288
Met Met Ala Lys Arg Arg Arg Ile Gly Ser Leu Ile His Arg Leu His	
85 90 95	

aag cta aac cag gcg gcc agt gcc acg ccc aat cac ctg gag aag atc	336
Lys Leu Asn Gln Ala Ala Ser Ala Thr Pro Asn His Leu Glu Lys Ile	
100 105 110	

gag agg gaa aac caa ctg gat agg tat gtc gcc agg tcc ttt aga aat	384
Glu Arg Glu Asn Gln Leu Asp Arg Tyr Val Ala Arg Ser Phe Arg Asn	
115 120 125	

gcc gcc tac gga gtg att tgt gcc tcg gcc ata gcg ccc atg ttg ctt	432
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Ala Ala Tyr Gly Val Ile Cys Ala Ser Ala Ile Ala Pro Met Leu Leu	
130 135 140	
ggc ctg tgg gga tat gtg gag acg ggt gta ttt acc ccg acc aca ccc	480
Gly Leu Trp Gly Tyr Val Glu Thr Gly Val Phe Thr Pro Thr Thr Pro	
145 150 155 160	
atg gag ttc aac ttc tgg ctg gac gag cga aag cct cac ttt tat tgg	528
Met Glu Phe Asn Phe Trp Leu Asp Glu Arg Lys Pro His Phe Tyr Trp	
165 170 175	
ccc atc tac gtt tgg ggc gta ctg ggc gtg gca gct gcc gcc tgg ttg	576
Pro Ile Tyr Val Trp Gly Val Leu Gly Val Ala Ala Ala Ala Trp Leu	
180 185 190	
gcc att gca acg gac acc ctg ttc tcc tgg ctg act cac aat gtg gtg	624
Ala Ile Ala Thr Asp Thr Leu Phe Ser Trp Leu Thr His Asn Val Val	
195 200 205	
att cag ttc caa cta ctg gag ctt gtt ctc gaa gag aag gat ctg aat	672
Ile Gln Phe Gln Leu Leu Glu Leu Val Leu Glu Glu Lys Asp Leu Asn	
210 215 220	
ggc gga gac tct cgc ctg acc ggg ttt gtt agt cgt cat cgt ata gct	720
Gly Gly Asp Ser Arg Leu Thr Gly Phe Val Ser Arg His Arg Ile Ala	
225 230 235 240	
ctg gat ttg gcc aag gaa cta agt tcg att ttc ggg gag atc gtc ttt	768
Leu Asp Leu Ala Lys Glu Leu Ser Ser Ile Phe Gly Glu Ile Val Phe	
245 250 255	
gtg aaa tac atg ctc agt tac ctg caa ctc tgc atg ttg gcc ttt cgc	816
Val Lys Tyr Met Leu Ser Tyr Leu Gln Leu Cys Met Leu Ala Phe Arg	
260 265 270	
ttc agc cgc agt ggc tgg agt gcc cag gtg cca ttt aga gcc acc ttc	864
Phe Ser Arg Ser Gly Trp Ser Ala Gln Val Pro Phe Arg Ala Thr Phe	
275 280 285	
cta gtg gcc atc atc atc caa ctg agt tcg tat tgc tat gga ggc gag	912
Leu Val Ala Ile Ile Ile Gln Leu Ser Ser Tyr Cys Tyr Gly Gly Glu	
290 295 300	
tat ata aag cag caa agt ttg gcc atc gca caa gcc gtt tat ggt caa	960
Tyr Ile Lys Gln Gln Ser Leu Ala Ile Ala Gln Ala Val Tyr Gly Gln	
305 310 315 320	
atc aat tgg cca gaa atg acg cca aag aaa aga aga ctc tgg caa atg	1008

Gly Leu Trp Gly Tyr Val Glu Thr Gly Val Phe Thr Pro Thr Thr Pro
 145 150 155 160

Met Glu Phe Asn Phe Trp Leu Asp Glu Arg Lys Pro His Phe Tyr Trp
 165 170 175

Pro Ile Tyr Val Trp Gly Val Leu Gly Val Ala Ala Ala Ala Trp Leu
 180 185 190

Ala Ile Ala Thr Asp Thr Leu Phe Ser Trp Leu Thr His Asn Val Val
 195 200 205

Ile Gln Phe Gln Leu Leu Glu Leu Val Leu Glu Glu Lys Asp Leu Asn
 210 215 220

Gly Gly Asp Ser Arg Leu Thr Gly Phe Val Ser Arg His Arg Ile Ala
 225 230 235 240

Leu Asp Leu Ala Lys Glu Leu Ser Ser Ile Phe Gly Glu Ile Val Phe
 245 250 255

Val Lys Tyr Met Leu Ser Tyr Leu Gln Leu Cys Met Leu Ala Phe Arg
 260 265 270

Phe Ser Arg Ser Gly Trp Ser Ala Gln Val Pro Phe Arg Ala Thr Phe
 275 280 285

Leu Val Ala Ile Ile Ile Gln Leu Ser Ser Tyr Cys Tyr Gly Gly Glu
 290 295 300

Tyr Ile Lys Gln Gln Ser Leu Ala Ile Ala Gln Ala Val Tyr Gly Gln
 305 310 315 320

Ile Asn Trp Pro Glu Met Thr Pro Lys Lys Arg Arg Leu Trp Gln Met
 325 330 335

Val Ile Met Arg Ala Gln Arg Pro Ala Lys Ile Phe Gly Phe Met Phe
 340 345 350

Val Val Asp Leu Pro Leu Leu Leu Trp Val Ile Arg Thr Ala Gly Ser
 355 360 365

Phe Leu Ala Met Leu Arg Thr Phe Glu Arg
 370 375

<210> 85
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 <212> DNA
 <213> Drosophila melanogaster

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 <222> (1)..(1065)
 <223> DORLU 16.1

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 1 5 10 15

atg ttc aag acc ctt ggc tac gat cta ttc cat aca ccc aaa ccc tgg 96
 Met Phe Lys Thr Leu Gly Tyr Asp Leu Phe His Thr Pro Lys Pro Trp
 20 25 30

tgg cgc tat ctg ctt gtg cga gga tac ttc gtt ttg tgc acg atc agc 144
 Trp Arg Tyr Leu Leu Val Arg Gly Tyr Phe Val Leu Cys Thr Ile Ser
 35 40 45

aac ttt tac gag gct tcc atg gtg acg aca agg ata att gag tgg gaa 192
 Asn Phe Tyr Glu Ala Ser Met Val Thr Thr Arg Ile Ile Glu Trp Glu
 50 55 60

tcc ttg gcc gga agt ccc tcc aaa ata atg cga cag ggt ctg cac ttc 240
 Ser Leu Ala Gly Ser Pro Ser Lys Ile Met Arg Gln Gly Leu His Phe
 65 70 75 80

ttt tac atg ttg agt agc caa ttg aaa ttt atc aca ttc atg ata aat 288
 Phe Tyr Met Leu Ser Ser Gln Leu Lys Phe Ile Thr Phe Met Ile Asn
 85 90 95

cgc aaa cgc cta ctg cag ctg agc cat cgt ttg aaa gag ttg tat cct 336
 Arg Lys Arg Leu Leu Gln Leu Ser His Arg Leu Lys Glu Leu Tyr Pro
 100 105 110

cat aaa gag caa aat caa agg aag tac gag gtg aat aaa tac tac cta 384
 His Lys Glu Gln Asn Gln Arg Lys Tyr Glu Val Asn Lys Tyr Tyr Leu
 115 120 125

tcc tgt tcc acg cgc aat gtt ttg tac gtg tac tac ttt gta atg gtc 432
 Ser Cys Ser Thr Arg Asn Val Leu Tyr Val Tyr Tyr Phe Val Met Val
 130 135 140

gtc atg gca ctg gaa ccc ctc gtt cag tcg tgc att atc cag ttc ata 480

Val Met Ala Leu Glu Pro Leu Val Gln Ser Cys Ile Ile Gln Phe Ile	
145	150 155 160
gtg aat gtg agc ctg ggc aca gat ctg tgg atg atg tgc gtc tca agc	528
Val Asn Val Ser Leu Gly Thr Asp Leu Trp Met Met Cys Val Ser Ser	
165	170 175
caa ata tcg atg cac ttg ggc tat ctg gcc aat atg ttg gcc tcc att	576
Gln Ile Ser Met His Leu Gly Tyr Leu Ala Asn Met Leu Ala Ser Ile	
180	185 190
cga cca agt cca gaa acg gaa caa caa gac tgt gac ttc ttg gcc agc	624
Arg Pro Ser Pro Glu Thr Glu Gln Gln Asp Cys Asp Phe Leu Ala Ser	
195	200 205
att ata aag aga cat caa cta atg atc agg ctt caa aag gac gtg aac	672
Ile Ile Lys Arg His Gln Leu Met Ile Arg Leu Gln Lys Asp Val Asn	
210	215 220
tat gtt ttt gga ctc tta ttg gca tct aat ctg ttt acc aca tcc tgt	720
Tyr Val Phe Gly Leu Leu Leu Ala Ser Asn Leu Phe Thr Thr Ser Cys	
225	230 235 240
tta ctt tgc tgc atg gcg tac tat acc gtc gtc gaa ggt ttc aat tgg	768
Leu Leu Cys Cys Met Ala Tyr Tyr Thr Val Val Glu Gly Phe Asn Trp	
245	250 255
gag ggc att tcc tat atg atg ctc ttt gct agt gta gct gcc cag ttc	816
Glu Gly Ile Ser Tyr Met Met Leu Phe Ala Ser Val Ala Ala Gln Phe	
260	265 270
tac gtt gtc agc tca cac gga caa atg tta ata gat ttg agt aca aat	864
Tyr Val Val Ser Ser His Gly Gln Met Leu Ile Asp Leu Ser Thr Asn	
275	280 285
tta gcc aag gct gcc ttt gaa agc aag tgg tat gaa gga tct ttg cga	912
Leu Ala Lys Ala Ala Phe Glu Ser Lys Trp Tyr Glu Gly Ser Leu Arg	
290	295 300
taq aaa aag gag ata ctc att cta atg gca cag gct caa cga cct ttg	960
Tyr Lys Lys Glu Ile Leu Ile Leu Met Ala Gln Ala Gln Arg Pro Leu	
305	310 315 320
gag att tca gcc agg gga gta att atc ata tcc ctc gac acc ttt aaa	1008
Glu Ile Ser Ala Arg Gly Val Ile Ile Ile Ser Leu Asp Thr Phe Lys	
325	330 335
ata ttg atg acc atc aca tac aga ttt ttc gcg gtt ata cga caa act	1056

Ile Leu Met Thr Ile Thr Tyr Arg Phe Phe Ala Val Ile Arg Gln Thr
 340 345 350

gta gaa aag
 Val Glu Lys
 355

1065

<210> 86
 <211> 355
 <212> PRT
 <213> Drosophila melanogaster

<400> 86
 Met Glu Lys Leu Arg Ser Tyr Glu Asp Phe Ile Phe Met Ala Asn Met
 1 5 10 15

Met Phe Lys Thr Leu Gly Tyr Asp Leu Phe His Thr Pro Lys Pro Trp
 20 25 30

Trp Arg Tyr Leu Leu Val Arg Gly Tyr Phe Val Leu Cys Thr Ile Ser
 35 40 45

Asn Phe Tyr Glu Ala Ser Met Val Thr Thr Arg Ile Ile Glu Trp Glu
 50 55 60

Ser Leu Ala Gly Ser Pro Ser Lys Ile Met Arg Gln Gly Leu His Phe
 65 70 75 80

Phe Tyr Met Leu Ser Ser Gln Leu Lys Phe Ile Thr Phe Met Ile Asn
 85 90 95

Arg Lys Arg Leu Leu Gln Leu Ser His Arg Leu Lys Glu Leu Tyr Pro
 100 105 110

His Lys Glu Gln Asn Gln Arg Lys Tyr Glu Val Asn Lys Tyr Tyr Leu
 115 120 125

Ser Cys Ser Thr Arg Asn Val Leu Tyr Val Tyr Tyr Phe Val Met Val
 130 135 140

Val Met Ala Leu Glu Pro Leu Val Gln Ser Cys Ile Ile Gln Phe Ile
 145 150 155 160

Val Asn Val Ser Leu Gly Thr Asp Leu Trp Met Met Cys Val Ser Ser
 165 170 175

Gln Ile Ser Met His Leu Gly Tyr Leu Ala Asn Met Leu Ala Ser Ile

005240-4515900

180	185	190
Arg Pro Ser Pro Glu Thr Glu Gln Gln Asp Cys Asp Phe Leu Ala Ser		
195	200	205
Ile Ile Lys Arg His Gln Leu Met Ile Arg Leu Gln Lys Asp Val Asn		
210	215	220
Tyr Val Phe Gly Leu Leu Leu Ala Ser Asn Leu Phe Thr Thr Ser Cys		
225	230	235 240
Leu Leu Cys Cys Met Ala Tyr Tyr Thr Val Val Glu Gly Phe Asn Trp		
	245	250 255
Glu Gly Ile Ser Tyr Met Met Leu Phe Ala Ser Val Ala Ala Gln Phe		
	260	265 270
Tyr Val Val Ser Ser His Gly Gln Met Leu Ile Asp Leu Ser Thr Asn		
	275	280 285
Leu Ala Lys Ala Ala Phe Glu Ser Lys Trp Tyr Glu Gly Ser Leu Arg		
	290	295 300
Tyr Lys Lys Glu Ile Leu Ile Leu Met Ala Gln Ala Gln Arg Pro Leu		
305	310	315 320
Glu Ile Ser Ala Arg Gly Val Ile Ile Ile Ser Leu Asp Thr Phe Lys		
	325	330 335
Ile Leu Met Thr Ile Thr Tyr Arg Phe Phe Ala Val Ile Arg Gln Thr		
	340	345 350
Val Glu Lys		
355		

<210> 87
 <211> 1272
 <212> DNA
 <213> Drosophila melanogaster

<220>
 <221> CDS
 <222> (1)..(1272)
 <223> DORLU 22.1

<400> 87

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Asn Tyr Ile Ile Ser Tyr Phe Trp Asn Val Cys Ala Ala Leu Gly Val	
195 200 205	
gca ctg ccc acc gtt tgt gtg gac aca ctg ttc tgt tct ctg agc cat	672
Ala Leu Pro Thr Val Cys Val Asp Thr Leu Phe Cys Ser Leu Ser His	
210 215 220	
aat ctc tgt gcc cta ttc cag att gcc agg cac aaa atg atg cac ttt	720
Asn Leu Cys Ala Leu Phe Gln Ile Ala Arg His Lys Met Met His Phe	
225 230 235 240	
gag ggc aga aat acc aaa gag act cat gag aac tta aag cac gtg ttt	768
Glu Gly Arg Asn Thr Lys Glu Thr His Glu Asn Leu Lys His Val Phe	
245 250 255	
caa cta tat gcg ttg tgt ttg aac ctg gcc cat ttc tta aac gaa tat	816
Gln Leu Tyr Ala Leu Cys Leu Asn Leu Gly His Phe Leu Asn Glu Tyr	
260 265 270	
ttc aga cgc ctc atc tgc cag ttt gtg gca gcc tca ctg cac ttg tgt	864
Phe Arg Pro Leu Ile Cys Gln Phe Val Ala Ala Ser Leu His Leu Cys	
275 280 285	
gtc ctg tgc tac caa ctg tct gcc aat atc ctg cag cca gcg tta ctc	912
Val Leu Cys Tyr Gln Leu Ser Ala Asn Ile Leu Gln Pro Ala Leu Leu	
290 295 300	
ttc tat gcc gca ttt acg gca gca gtt gtt ggc cag gtg tct ata tac	960
Phe Tyr Ala Ala Phe Thr Ala Ala Val Val Gly Gln Val Ser Ile Tyr	
305 310 315 320	
tgc ttc tgc gga tcg agc atc cat tcg gag tgt cag cta ttt ggc cag	1008
Cys Phe Cys Gly Ser Ser Ile His Ser Glu Cys Gln Leu Phe Gly Gln	
325 330 335	
gcc atc tac gag tcc agc tgg ccc cat ctg ctg cag gaa aac ctg cag	1056
Ala Ile Tyr Glu Ser Ser Trp Pro His Leu Leu Gln Glu Asn Leu Gln	
340 345 350	
ctt gta agc tcc tta aaa att gcc atg atg cga tcg agt ttg gga tgt	1104
Leu Val Ser Ser Leu Lys Ile Ala Met Met Arg Ser Ser Leu Gly Cys	
355 360 365	
ccc atc gat ggt tac ttc ttc gag gcc aat cgg gag acg ctc atc acg	1152
Pro Ile Asp Gly Tyr Phe Phe Glu Ala Asn Arg Glu Thr Leu Ile Thr	
370 375 380	

atc cct ggc cta gct ttc cgg gct ttc att att cag tgg ttc agt cgt 1200
 Ile Pro Gly Leu Ala Phe Arg Ala Phe Ile Ile Gln Trp Phe Ser Arg
 385 390 395 400

tcg ggt ttg ttt aac tcc gga aat att tac aat tat gct tta agc cgg 1248
 Ser Gly Leu Phe Asn Ser Gly Asn Ile Tyr Asn Tyr Ala Leu Ser Arg
 405 410 415

tgt tgt tac agc cag ttg gct aat 1272
 Cys Cys Tyr Ser Gln Leu Ala Asn
 420

<210> 88

<211> 424

<212> PRT

<213> *Drosophila melanogaster*

<400> 88

Met Leu Thr Asp Lys Phe Leu Arg Leu Gln Ser Ala Leu Phe Arg Leu
 1 5 10 15

Leu Gly Leu Glu Leu Leu His Glu Gln Asp Val Gly His Arg Tyr Pro
 20 25 30

Trp Arg Ser Ile Cys Cys Ile Leu Ser Val Ala Ser Phe Met Pro Leu
 35 40 45

Thr Ile Ala Phe Gly Leu Gln Asn Val Gln Asn Val Glu Gln Leu Thr
 50 55 60

Asp Ser Leu Cys Ser Val Leu Val Asp Leu Leu Ala Leu Cys Lys Ile
 65 70 75 80

Gly Leu Phe Leu Trp Leu Tyr Lys Asp Phe Lys Phe Leu Ile Gly Gln
 85 90 95

Phe Tyr Cys Val Leu Gln Thr Glu Thr His Thr Ala Val Ala Glu Met
 100 105 110

Ile Val Thr Arg Glu Ser Arg Arg Asp Gln Phe Ile Ser Ala Met Tyr
 115 120 125

Ala Tyr Cys Phe Ile Thr Ala Gly Leu Ser Ala Cys Leu Met Ser Pro
 130 135 140

Leu Ser Met Leu Ile Ser Tyr His Glu Gln Val Asn Cys Ser Arg Asn
 145 150 155 160

00540 2516160

003270 254600

Phe His Phe Pro Val Cys Lys Lys Lys Tyr Cys Leu Ile Ser Arg Ile
165 170 175

Leu Arg Tyr Ser Phe Cys Arg Tyr Pro Trp Asp Asn Met Lys Leu Ser
180 185 190

Asn Tyr Ile Ile Ser Tyr Phe Trp Asn Val Cys Ala Ala Leu Gly Val
195 200 205

Ala Leu Pro Thr Val Cys Val Asp Thr Leu Phe Cys Ser Leu Ser His
210 215 220

Asn Leu Cys Ala Leu Phe Gln Ile Ala Arg His Lys Met Met His Phe
225 230 235 240

Glu Gly Arg Asn Thr Lys Glu Thr His Glu Asn Leu Lys His Val Phe
245 250 255

Gln Leu Tyr Ala Leu Cys Leu Asn Leu Gly His Phe Leu Asn Glu Tyr
260 265 270

Phe Arg Pro Leu Ile Cys Gln Phe Val Ala Ala Ser Leu His Leu Cys
275 280 285

Val Leu Cys Tyr Gln Leu Ser Ala Asn Ile Leu Gln Pro Ala Leu Leu
290 295 300

Phe Tyr Ala Ala Phe Thr Ala Ala Val Val Gly Gln Val Ser Ile Tyr
305 310 315 320

Cys Phe Cys Gly Ser Ser Ile His Ser Glu Cys Gln Leu Phe Gly Gln
325 330 335

Ala Ile Tyr Glu Ser Ser Trp Pro His Leu Leu Gln Glu Asn Leu Gln
340 345 350

Leu Val Ser Ser Leu Lys Ile Ala Met Met Arg Ser Ser Leu Gly Cys
355 360 365

Pro Ile Asp Gly Tyr Phe Phe Glu Ala Asn Arg Glu Thr Leu Ile Thr
370 375 380

Ile Pro Gly Leu Ala Phe Arg Ala Phe Ile Ile Gln Trp Phe Ser Arg
385 390 395 400

Ser Gly Leu Phe Asn Ser Gly Asn Ile Tyr Asn Tyr Ala Leu Ser Arg
405 410 415

Cys Cys Tyr Ser Gln Leu Ala Asn
420

<210> 89
<211> 1176
<212> DNA
<213> Drosophila melanogaster

<220>
<221> CDS
<222> (1)..(1176)
<223> DORLU 24.1

<400> 89
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Met Ser Lys Leu Ile Glu Val Phe Leu Gly Asn Leu Trp Thr Gln Arg
1 5 10 15

ttt acc ttc gcc cga atg ggt ttg gat ttg cag ccc gat aaa aag ggc 96
Phe Thr Phe Ala Arg Met Gly Leu Asp Leu Gln Pro Asp Lys Lys Gly
20 25 30

aat gtt ttg cga tct ccg ctt ctt tat tgt att atg tgt ctg aca aca 144
Asn Val Leu Arg Ser Pro Leu Leu Tyr Cys Ile Met Cys Leu Thr Thr
35 40 45

agc ttt gag ctc tgc acc gtg tgc gcc ttt atg gtc caa aat cgc aac 192
Ser Phe Glu Leu Cys Thr Val Cys Ala Phe Met Val Gln Asn Arg Asn
50 55 60

caa atc gtg ctt tgt tcc gag gcc ctg atg cac gga cta cag atg gtc 240
Gln Ile Val Leu Cys Ser Glu Ala Leu Met His Gly Leu Gln Met Val
65 70 75 80

tcc tcg cta ctg aag atg gct ata ttc ttg gcc aaa tct cac gac ctg 288
Ser Ser Leu Leu Lys Met Ala Ile Phe Leu Ala Lys Ser His Asp Leu
85 90 95

gtg gac cta att caa cag att cag tcg cct ttt aca gag gag gat ctt 336
Val Asp Leu Ile Gln Gln Ile Gln Ser Pro Phe Thr Glu Glu Asp Leu
100 105 110

gta ggt aca gag tgg aga tcc caa aat caa agg gga caa cta atg gct 384
Val Gly Thr Glu Trp Arg Ser Gln Asn Gln Arg Gly Gln Leu Met Ala
115 120 125

gcc att tac ttt atg atg tgt gcc ggt acg agt gtg tca ttt ctg ttg	432
Ala Ile Tyr Phe Met Met Cys Ala Gly Thr Ser Val Ser Phe Leu Leu	
130 135 140	
atg cca gtg gct ttg acc atg ctt aag tac cat tcc act ggg gaa ttc	480
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Phe Phe Cys Cys Ser Thr Thr Gly Val Asp Thr Leu Tyr Gly Trp Cys	
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Gly Ile Phe Val Glu His Ala Arg Leu Leu Lys Ile Val Gln His Phe	
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Asn Tyr Ser Phe Met Glu Ile Ala Phe Val Glu Val Val Ile Ile Cys	
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Gly Leu Tyr Cys Ser Val Ile Cys Gln Tyr Ile Met Pro His Thr Asn	
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Gln Asn Phe Ala Phe Leu Gly Phe Phe Ser Leu Val Val Thr Thr Gln	
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Leu Cys Ile Tyr Leu Phe Gly Ala Glu Gln Val Arg Leu Glu Ala Glu	
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Ala Pro Val Ser Ser Phe Arg Val Leu Leu Pro Tyr Asp Val Thr Gln	165	170	175
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Asn Tyr Ser Phe Met Glu Ile Ala Phe Val Glu Val Val Ile Ile Cys	260	265	270
Gly Leu Tyr Cys Ser Val Ile Cys Gln Tyr Ile Met Pro His Thr Asn	275	280	285
Gln Asn Phe Ala Phe Leu Gly Phe Phe Ser Leu Val Val Thr Thr Gln	290	295	300
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Pro Lys His Arg Lys Leu Phe Leu Phe Pro Ile Glu Arg Ala Gln Arg	340	345	350
Glu Thr Val Leu Gly Ala Tyr Phe Phe Glu Leu Gly Arg Pro Leu Leu	355	360	365

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 Tyr Pro Phe Gly Tyr Tyr Val Asn Gly Ser Gly Val Leu Ala Val Leu
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 Val Arg Phe Cys Asp Leu Thr Tyr Glu Leu Phe Asn Tyr Phe Val Ser
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 Val His Ile Ala Gly Leu Tyr Ile Cys Thr Ile Tyr Ile Asn Tyr Gly
 65 70 75 80
 caa ggc gat ttg gac ttc ttc gtg aac tgt ttg ata caa acc att att 288
 Gln Gly Asp Leu Asp Phe Phe Val Asn Cys Leu Ile Gln Thr Ile Ile
 85 90 95
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 Tyr Leu Trp Thr Ile Ala Met Lys Leu Tyr Phe Arg Arg Phe Arg Pro
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Gln His His Arg Tyr Ile Val Ala Ala Leu Lys Lys Ile Glu Ser Phe	
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Tyr Ser Pro Ile Trp Phe Val Lys Ile Gly Glu Val Thr Phe Leu Met	
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Cys Leu Val Ala Phe Val Ser Thr Lys Ser Thr Ala Ala Asn Ser Phe	
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Arg Cys Gly Glu Ala Leu Trp Arg Ser Pro Trp Gln Arg His Leu Lys	
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Asp Val Arg Ser Asp Tyr Met Phe Phe Met Leu Asn Ser Arg Arg Gln	
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Phe Gln Leu Thr Ala Gly Lys Ile Ser Asn Leu Asn Val Asp Arg Phe	
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Val Arg Phe Cys Asp Leu Thr Tyr Glu Leu Phe Asn Tyr Phe Val Ser	50	55	60
Val His Ile Ala Gly Leu Tyr Ile Cys Thr Ile Tyr Ile Asn Tyr Gly	65	70	75
Gln Gly Asp Leu Asp Phe Phe Val Asn Cys Leu Ile Gln Thr Ile Ile	85	90	95
Tyr Leu Trp Thr Ile Ala Met Lys Leu Tyr Phe Arg Arg Phe Arg Pro	100	105	110
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Met Ser Lys Leu Trp Ile Lys Thr Tyr Val Tyr Cys Cys Tyr Ile Gly	145	150	155
Thr Ile Phe Trp Leu Ala Leu Pro Ile Ala Tyr Arg Asp Arg Ser Leu	165	170	175
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Ser Ser Tyr Val Leu Met Gly Ala Asn Met Thr Glu Leu Asn Gln Leu	245	250	255
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Arg	Ile	Asn	Phe	Trp	Pro	Leu	Ser	Ala	Gly	Phe	Phe	Thr	Cys	Thr	Thr	
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Lys	Val	Leu	Leu	Asn	Tyr	Pro	Phe	Phe	Pro	Leu	Thr	Tyr	Ile	Phe	Ile	
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Gln	Ala	Glu	Ile	Glu	Ser	Met	Phe	Arg	Pro	Tyr	Thr	Asp	His	Leu	Glu	
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 Val Ile Phe Phe Ala Ser Met Ser Phe Gly Leu Thr Glu Ser Met Gly
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 Asp His Val Gln Met Gly Arg Asp Leu Ala Phe Ile Leu Gly Thr Tyr
 50 55 60

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Val	Leu	Met	Leu	Leu	Ala	Leu	Gly	His	Leu	Ser	Met	Trp	Ser	Tyr	Cys		
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Glu	Ala	Tyr	Asp	Pro	Thr	Lys	Gly	Ser	Lys	Asp	Val	Tyr	Arg	Asp	Leu		
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Thr Leu Lys Leu Met Lys Phe Trp Ser Tyr Leu Phe Val His Asn Trp	
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Arg Arg Tyr Val Ala Met Thr Pro Tyr Ile Ile Ile Asn Cys Thr Gln	
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198

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<222> (1223)..(1283)

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